Compliments of
PIERRE A. FISH

ABSTRACTS

OF

WORK DONE IN THE LABORATORY

OF

VETERINARY PHYSIOLOGY AND
. . . . PHARMACOLOGY . . . .

UNDER THE DIRECTION OF P. A. FISH

NO. 1

NEW YORK STATE VETERINARY COLLEGE
CORNELL UNIVERSITY
ITHACA, N. Y.
1904

New York State Veterinary College. Clinic. Hospital. Observatory.

TABLE OF CONTENTS

PREFATORY NOTE.

As indicated by the title of this pamphlet, it is proposed to publish abstracts of the longer scientific articles written in this department. Short articles will be published entire. In certain cases reprints of articles published in other journals are included; but other papers will appear here for the first time.

Such a collection, annually in a single pamphlet, it is believed will present certain advantages from the standpoint of the department, in that some record of all the work will be available in a compact and convenient form.

It is also planned to publish short articles on methods, tests and technique, bearing upon physiologic and pharmacologic work. Such articles have a value of their own; but at the present time, unfortunately, in this country there is a dearth or complete absence of journals where such work may be presented.

Finally the department desires to keep in touch with its alumni and others interested in its work, and to this end invites suggestions.

May 1, 1904. P. A. F.

DEPARTMENT COURSES

PHYSIOLOGY

P. A. Fish, Professor — H. J. Milks, Assistant
W. B. Mack, Assistant

It is the aim of this department to select from a wide field of important topics, those which will be of greater use to the student, in comprehending the vital processes of the animal body. Without a complete understanding of the normal functions, it is obviously useless to attempt progress in the proper conception of diseased conditions.

The proper correlation of work in the laboratory, recitation and lecture room, it is believed will afford to the student a more comprehensive grasp and understanding of the perspective and symmetry of a subject than can otherwise be obtained.

The lectures are illustrated with lantern slides, charts, histological preparations, dissections and practical demonstrations relative to the subject under discussion.

The department has a good library of modern elementary and advanced text books on physiology and students are urged to make the fullest use of it in connection with the lecture and laboratory courses.

The laboratory is located on the second floor of the Veterinary College. It is well lighted and ventilated and equipped with new apparatus. The equipment includes kymographs, induction coils, sphygmographs, cardiographs, circulation schemas, tambours, centrifuges, microscopes, and other apparatus for complete and satisfactory work.

Every encouragement is offered, to those properly fitted, to pursue their work beyond that given in the regular course.

Courses

20. Physiology Recitations.—Two hours weekly. First Term. Two sections. Section I, M., 9, T., 10. Section II, T., 11, W., 10. Drs. Fish, Milks and Mack.

20. a. Physiology Recitations.—One hour weekly. Second term. Two sections. S. 10, 11. Drs. Fish, Milks and Mack.

21. Physiology Lectures.—Three hours weekly. Second term. T., Th., F., 10. Dr. Fish.

22. **Physiological Laboratory.**—A portion of the course is devoted to chemical physiology. Artificial digestive juices are tested upon the various kinds of foodstuffs by the students and careful notes kept of the various changes. Milk, Bile and Blood are also studied including a spectroscopic examination of the latter. A large proportion of the work is devoted to a study of the phenomena associated with the circulatory, respiratory, muscular and nervous systems. Students are to obtain and preserve graphic records of these phenomena, whenever possible. Certain experiments requiring special apparatus and care are performed by the instructors, as demonstrations, students assisting when possible. Five hours each week, second term. Section I, T. 11–1, W. 2–5. Section II, Th., 11–1, F. 8–10, 11–12. Drs. FISH, MILKS and MACK.

23. **Course in Urine Analysis.**—Laboratory work devoted to the comparative study of urine. Examinations are made of human urine and that of the domestic animals, especially the horse. In addition to the chemical examination some time will be devoted to a microscopic study of urinary deposits. So far as possible each student is expected to prepare and preserve a series of "typical slides." Five hours weekly, first term. W., 10–1, S., 11–1, September–December. Drs. FISH, MILKS and MACK.

24. **Research and Thesis.**—7½ hours per week throughout the year. This course includes advanced work, independent of the thesis and reports of progress are given at the department seminary every fortnight. Drs. FISH, MILKS and MACK.

PHARMACOLOGY

P. A. FISH, Professor H. J. MILKS, Assistant
W. B. MACK, Assistant

The term is employed in its comprehensive meaning to include not only the materials of medicine, but their preparation, use and physiological action. Allowing for certain exceptional differences, there is, in general, a resemblance in the action of drugs in the lower animals and in human beings.

The clinics furnish abundant material for the use of medicines and the study of their actions.

The physiological changes in certain tissues resulting from the toxic doses of many drugs is as yet unknown, and opportunities for research are abundant in this field.

25. **Pharmacology.**—A study of the actions and uses of the various drugs and their preparation. A varied collection of the crude

drugs and their official preparations is available and examined at the lectures. The course is conducted in the form of lectures with short weekly examinations. First term. Th., F., 10. Dr. Fish.

26. **Materia Medica and Pharmacy Laboratory.**—The work in this course consists of the study of a selected group of inorganic drugs; the study of certain crude organic drugs and their official preparations; in making pharmaceutical preparations, such as syrups, emulsions, spirits, liniments, tinctures, fluid extracts, extracts, ointments, pills and others. Some exercises will also be devoted to the study of the direct physiological action of a few selected drugs upon some of the lower animals.

In their study the students are required to write concise notes of the physiological action of the drugs examined and to make tests of their incompatibility. In addition to this each student will have practical experience in writing and compounding prescriptions. The importance of a discriminating and accurate system for dispensing medicines is thoroughly emphasized. Five hours each week. First term. Sect. I, W., 2–5, Th., 11–1. Sect. II, M., 10–1, Tu., 10–1. Drs. Fish, Milks and Mack.

27. **Clinical Diagnosis and Therapeutics.**—Two recitations per week in Diagnosis for the first half of the first term. S., M., 10. Dr. Fish. The recitations will be supplemented by practical experience in the medical clinics.

Therapeutics.—The treatment and cure of disease. This subject, standing along with pathology, unites physiology, anatomy, chemistry and botany with medicine and surgery. It is therefore necessary to have some knowledge of these branches in order to obtain a full appreciation of the means employed in the restoration of health.

This course must be preceded by the first and second years course in physiology and pharmacology, or their equivalents. Two lectures each week second half of the first term. S. and M., 10. Dr. Fish.

28. **Recitations in Materia Medica.**—Second term. M., W., 10 A. M. Dr. Fish.

29. **Research and Thesis.**—7½ hours weekly throughout the year. This course includes advanced work independent of the thesis and reports of progress are given at the department seminary every fortnight. Drs. Fish, Milks and Mack.

[Reprinted from the AMERICAN VETERINARY REVIEW, November, 1903.]

ECHINACEA IN VETERINARY PRACTICE.

BY P. A. FISH, ~~M. D.~~, M. D. V., ITHACA, N. Y.

A Paper read before the 13th Annual Meeting of the New York State Veterinary Medical Society, at Ithaca, Sept. 15-16, 1903.

Echinacea angustifolia, De Candolle, is an herbaceous plant, the root of which sends up from year to year a slender, but sometimes a rather stout, stem, two or three feet in height, bristling with hairs. It is an indigenous plant growing chiefly in the Western States, from Illinois to Nebraska, and southward through Missouri to Texas, thriving best in rich prairie soil. It is abundant in Kansas. The generic term, *Echinos*, meaning hedgehog or sea urchin, refers to the spiny, hedgehog-like fruiting head ; while the specific name angustifolia originates from the Latin words *angustus* (narrow) and *folium* (leaf), contrasting this species from the other forms of echinacea. It is quite distinct from *Echinacea purpurea*, Moench, which is a taller plant with wider leaves, growing in the Eastern States from Pennsylvania west. *Echinacea angustifolia* is the narrow-leaved variety and blooms from June to August. It belongs to the natural order compositæ and the root is the part used in medicine.

Synonyms.—Purple cone flower, cone flower, nigger-head, black sampson, the latter term also being employed for *E. purpurea.*

History.—Dr. H. F. C. Meyer, of Pawnee City, Nebraska, (1870), seems to have been the first among physicians to have used echinacea as a medicine. He used it in a secret mixture with wormwood and hops, and called it "Meyer's Blood Purifier." Among his claims for it was its antidotal action upon the poison of various insects, and particularly that of the rattlesnake. Dr. Meyer stated that he even allowed a rattler to bite him, after which he bathed the parts with some of the tincture, took a dram of it internally, and laid down and slept, and upon awakening all traces of swelling had disappeared. In 1885 and 1886 he sent specimens of the plant to Mr. C. G. Lloyd, who

identified it as *Echinacea angustifolia* of De Candolle. In 1886 Dr. Meyer communicated to the late Professor John King his uses of the drug as he had employed it for the preceding sixteen years. Among other things, success for his remedy was claimed in boils, internal abscesses, ulcerated sore throat, old ulcers, nasal and pharyngeal catarrh, various fevers, trichinosis, acne, eczema, and also colic in horses. Later use of the drug has to some extent substantiated many of the almost incredible claims of the introducer; for the conditions for which it was recommended might well be due to vitiation or dyscrasia of the blood, the very field in which echinacea has been found to be most useful.

Professor King took an active interest in the drug and after extensive experiments became convinced that it possessed great merit. It is due to Professor King more than anyone else, perhaps, that the drug became generally used among the eclectic and other practitioners.

It is said that much of the root collected has little medicinal value. The root collected in the marshes and lowlands east of the Mississippi is of this negative quality. The best quality is obtained from the prairie lands of Nebraska. Professor Lloyd's experience is that few drugs vary more in quality than crude echinacea. The root, if of good quality, when chewed, gives at first a sweetish taste, later becoming acrid and pungent, and finally leaving a persistent tingling sensation, followed by a peculiar numbness of the tongue and fauces, apparently intermediate in character between that produced by aconite and cocaine.

Chemical Composition.—According to the investigations of Professor Lloyd, the plant contains minute quantities of an alkaloid, which is devoid of color, and unimportant so far as its medicinal qualities are concerned. In his earlier investigations he failed to find the alkaloid. He finds that "the characteristic principles of the root are those substances linked to an acid organic body of a resinous character, nearly, if not quite colorless, and possessing, in an exalted degree, the persistently acrid

qualities of echinacea—so intensely that it is distressing to the taste, even in very small amount, when pure. The stinging sensation affects the tip of the tongue for hours. But small quantities of it are present, even in the best root—less than ½ to 1 per cent."

The writer, experimenting upon some tablets of the powdered extract of echinacea, was unable to find any evidence of the presence of an alkaloid, glucoside or neutral principle, but did find a resin of which about 70% was soluble in ether.

Preparations.—Fluid extract, tincture, and echafolta. According to Professor Lloyd, the best menstruum for the fluid extract and tincture is alcohol 4 parts and water 1 part. Both preparations mix well with water, and there is no very appreciable precipitation. Echafolta is described as a purified preparation of echinacea, free from coloring matters and extraneous substances, such as chlorophyll, extractive, and other "plant dirt." Another preparation put out by Battle & Co., of St. Louis, is known as Ecthol, and is said to contain the active principles of Echinacea and Thuja.

Dosage.—Echinacea is comparatively non-toxic. In human medicine the dose of the fluid extract and tincture is given at ¼ to 1 drachm; echafolta 4 to 8 minims every one to four hours. In veterinary practice the writer has used the powdered root in doses ranging from 2 to 8 drachms for horses and cows.

Physiologic Action.—The action of the drug upon the mouth has been variously described as resembling aconite, pyrethrum and xanthoxylum. The tingling sensation persists for some little time, even after the throat has been gargled. The flow of saliva is promoted. According to Ellingwood, diaphoresis soon occurs and a continuation of the remedy stimulates the kidneys to increased action. "All of the glandular organs seem to feel the stimulating influence and their functional activity is increased. The stomach is improved in its function, the appetite increases, the food is more perfectly digested, the bowels operate better, and absorption, assimilation and general nutrition are materially improved. It encourages secretion and excre-

tion, preventing further auto-intoxication, and quickly correcting the influence in the system of any that has occurred. It stimulates retrograde metabolism, or tissue waste more markedly than any other single remedy known. It influences the entire lymphatic system. Anæmic conditions improve with increased nerve tone." Professor Webster recommends it as a stimulant to the capillary circulation.

The writer has confirmed upon himself the eliminative action of echinacea with respect to urea. Determinations were made upon the afternoon urine for six days, and the average amount of urea obtained for this period. A dose, of 5 grains of the powdered extract of echinacea in tablet form, was then taken three times a day before meals for six days and urea determinations taken as before. The following cut is introduced for the purpose of comparing the two series of determinations. The lower curve represents the period when the drug was not taken ; the upper is the echinacea curve.

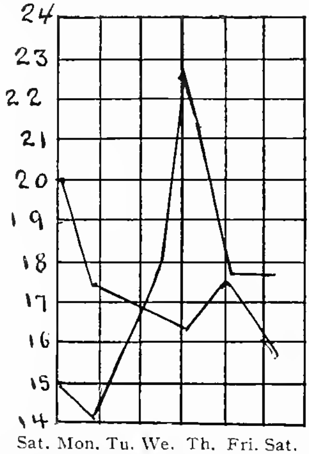


FIG. 1. The lower tracing represents the number of grammes of urea per 1000 c c. of urine for each of the six days when the echinacea was not taken. (Normal curve). The upper tracing represents similar condition when echinacea was taken.

The results showed that during the use of the echinacea there was an average increase of 2.83 grammes of urea per 1000 c.c. of afternoon urine, per day.

Some experiments were also tried upon kittens to determine

the toxicity of the drug, the fluid extract of echinacea and the preparation known as echafolta being used. Kittens weighing 2 and 2½ pounds were employed; one being dosed with two drachms of the fluid extract in six drachms of water; the other with two drachms of echafolta in six drachms of water. (The equivalent dose for a horse weighing 1000 pounds would be nearly 1 gallon of the drug). Within five minutes there was incoördination of movement and within twenty minutes both cats were unable to walk. There was some dilatation of the pupils during the early stages. After forty minutes emesis occurred, in the kitten which had received the fluid extract, and after this had occurred improvement took place, although lack of coördination persisted for some time. The following day this kitten was apparently as normal as ever. Emesis did not occur in the kitten receiving echafolta; she soon became quiet and lay upon her side as if asleep, but with her eyes open. The conjunctiva was less sensitive than normal and the pupils were somewhat contracted, but would still respond to light stimulus, although slowly. The appearances suggested a condition of profound narcosis or stupor, all of this occurring within two hours. The kitten remained in this condition all of the following day; but on the third day was found to be in her normal condition again.

Later the experiments were repeated under the same conditions, except that three drachms of each of the preparations were administered. The general symptoms were as before. On the second day the heart and respiration were much depressed, the body cold and the pupils contracted. The pulse fell to 56 and 58; respirations 10 and 12 and the temperature fell to 70.8 in one kitten and 71.8 in the other. The kitten receiving the fluid extract (there was no emesis this time) died toward the close of the second day. The kitten receiving the echafolta was found dead and in rigor on the morning of the third day. The post-mortems showed no marked changes aside from some congestion of the lungs, and the stomachs moderately distended with gas, some liquid, food and mucus were also found in the stomachs.

The suspicion arose that the effects above described might be due to the alcoholic menstrua in which the drugs were dissolved. Further experiments were therefore tried. The alcohol was driven off by evaporation until an extract of echafolta was obtained which was five times more concentrated than the normal drug. One drachm of this concentrated extract was mixed with 15 c.c. of distilled water and 5 c.c. of alcohol, and administered to a kitten as in the previous experiments. Compared with the first experiment, this kitten received 2½ times more of the echafolta, but with the alcohol driven off. There was apparently no effect during the 2½ hours she was under observation. The experiment was repeated upon a second kitten with similar results.

In another experiment, the alcohol was driven from the fluid extract of echinacea, until the resulting extract represented a concentration three times greater than the original fluid extract. Two drachms of this concentrated extract, mixed with 20 c. c. of water and 5 c.c. of alcohol, were administered to a kitten as in the case of echafolta; within ten minutes the kitten became uneasy and emesis occurred; four minutes later there was profuse salivation. An hour later the kitten was apparently normal again. In another experiment four drachms of the concentrated echinacea were administered in the usual way. Profuse salivation soon occurred and there were spasmodic movements of the body suggestive of attempts at vomiting. Within twelve minutes emesis took place and after this had occurred improvement set in and the kitten soon returned to its normal condition.

In still another experiment, one drachm of the powdered extract of echinacea, in tablet form, was mixed with four drachms of normal saline solution. This was divided into two portions and injected subcutaneously at four-minute intervals. Four minutes after the last injection, emesis occurred; no untoward symptoms occurred; the kitten continued to purr, but was not so playful as before. Three days later it was observed that abscesses were forming at the places of injection; in a day or two the abscesses broke and some sloughing of the tissues occurred.

Some days later the kitten was found dead, probably from infection. It should be stated that antiseptic precautions, in making the injections, were purposely omitted, as it is claimed by some that the drug possesses antiseptic properties. The result would indicate that the drug, without its alcoholic menstruum, has no inhibiting action upon the growth of bacteria.

To complete the observations, it remained to note the effects of alcohol and compare them with those produced by echinacea and echafolta. Three drachms of 95% alcohol diluted in water were administered to a kitten. Within ten minutes she showed signs of staggering. Incoördination of movement was not so marked and did not appear so promptly as when the drugs were used. She could still walk, but with difficulty, one hour later. The pupils varied in their condition, sometimes being contracted and at others dilated. The next day the cat was very much improved and soon recovered.

It should be pointed out that a three-drachm dose of the alcohol did not prove fatal, whereas the same dosage of either of the drug preparations caused the death of the animals on the second or third day. The narcotic effects were not so quickly produced nor so profound with the alcohol as with the drugs. The absence of effects from the drugs when deprived of their alcoholic menstrua may be explained by the fact that the drugs were practically insoluble in water and were therefore very slow in being absorbed; whereas, in the alcoholic menstruum, the drug was readily and quickly absorbed, so the whole bulk of the drug quickly entered the system and produced pronounced effects. With the drug in its insoluble form it entered the system so slowly and in such small amount that the effects were not noticeable.

Echinacea in tablet form, crushed and suspended in water and administered to frogs in proportionately large doses, produced quick narcotic effects from which the frog gradually recovered.

Human Therapeutics.—As a therapeutic agent echinacea or echafolta can be used internally and externally at the same time.

It is difficult to classify the drug under a single title. Some have referred to it as an alterative and as an antiseptic. The eclectic practitioners seem to agree in referring to it as a "corrector of the depravation of the body fluids."

It has been highly praised as a remedy for blood poisoning and changes manifested by a disturbed equilibrium of the body fluids, resulting in various tissue alterations exhibited as boils, carbuncles, abscesses, or cellular glandular inflammations.

It has been recommended for fevers resulting from the absorption of septic material, such as typhoid, puerperal, septicæmia, etc. It is regarded as a highly important remedy in uremic poisoning, diphtheria, various ulcerated and catarrhal conditions. Intestinal antisepsis, and aphrodisiac properties, when locally applied, are claimed for it. Satisfactory reports of its use have been given in appendicitis, erysipelas, spinal meningitis, cancerous growths, syphilis, tetanus, bites of poisonous animals and insects. The Sioux Indians have been reported as using the fresh root scraped and given freely for the bite of the rattlesnake with recovery in from two to twelve hours. Statements more difficult to accept are those in connection with rabies. It is said that in five or six cases, animals bitten at the same time as the patient, had developed rabies, and had even conveyed it to other animals, and yet the patient showed no evidence of poisoning, if the remedy was used at once. It is said that one case exhibited the developing symptoms of hydrophobia before the drug was used and that they shortly disappeared after treatment.

Veterinary Therapeutics.—Except for the reference, in the early part of this paper, to the use of echinacea for colic in horses, the drug has not been used in veterinary medicine, so far as the writer knows. The following cases seemed to be of the character for which the use of the drug was indicated, and it was therefore employed.

Case 1.—A small brown calf, weighing about seventy pounds, was brought to the clinic on account of loss of appetite, unthriftiness, and a peculiar grunt at the end of each expiration. Con-

stipation was marked ; some of the symptoms pointed toward impaction of the rumen, and there was some suspicion of pulmonary complications. For the first few days the calf did not improve. The constipation was quite resistant to treatment, although purgatives were administered at each end of the animal. Some echinacea was administered from the first. When the bowels were opened, echinacea in half-drachm doses, was the only treatment employed. The kidneys became active again (no urine had been observed for two or three days) ; the appetite became vigorous ; the expiratory grunt disappeared ; urination and defecation occurred freely, and the animal made an uneventful but satisfactory recovery. It is not unlikely that some auto-intoxication had occurred from the prolonged constipation with some respiratory complication.

Case 2.—A gelding, seven years old, weighing about 900 pounds, was brought to the clinic suffering from strangles. Pulse 48, temperature 104.4. A flaxseed poultice was applied to the intermaxillary swelling ; this was opened on the third day and about one-half ounce of pus escaped. One-drachm doses of powdered echinacea were administered from the outset, without other treatment. Within a week the pulse had fallen to 40 and the temperature to 100. The horse was discharged and no subsequent symptons appeared.

Case 3.—A Jersey cow suffering from fistulous withers. This cow had received treatment two months previously, and after four or five weeks had been sent home. Two weeks later she was returned, the fistula having broken out again, and her condition was such that it was thought best to give no further treatment, but to use her as a subject for dissection. While waiting for the dissection, the echinacea treatment was begun experimentally. Some necrotic tissue was removed from the tip of the scapula, and the fistula washed out daily with a solution consisting of one part of echafolta to twelve parts of water, and frequently some of the powdered echinacea was dusted over the wound. Internally two-drachm doses were given morning and night with the feed. A few days later the doses were raised to

one-half ounce, then to one ounce and for a short time she received two ounces at a single dose. The doses then dropped to one-half ounce until she was discharged cured. Upon inquiry, it was found that there was no recurrence of the trouble two or three months after her discharge. General improvement was noted soon after the treatment was inaugurated; her appetite increased and she began to put on flesh and there was general improvement in tone and vigor.

Case 4.—This case was reported to me by Dr. T. S. Childs, of Saratoga Springs, who used the drug in several cases of catarrhal fever "with more or less good results." The cases, however, were serious, and as the remedy was new and experimental he abandoned it in favor of his regular treatment. He writes, however, that he had one very bad case of the fever in which the echinacea was used throughout, with stimulants, and that it made a good recovery in a very short time.

Case 5.—Dr. J. B. McNeil, of Ballston Springs, writes me that he used echinacea in six cases of influenza and one case of purpura hæmorrhagica, the latter case being well advanced with some tissue disintegration. He gave one-drachm doses of echinacea every five hours and one-ounce doses of turpentine every six hours. He states that all of the cases made rapid recoveries, more especially the case of purpura hæmorrhagica, which he considered hopeless when he took it in charge.

Summary.—From the writer's observations it would appear that echinacea, in therapeutic doses, is a valuable agent for the elimination of morbid material from the system; that it exerts a beneficial effect upon the nutrition of the system, possibly through its eliminating action upon the waste material, thus causing a demand on the part of the tissues for new and better nourishment, as evidenced by a stimulated appetite. Its action may, in some respects, resemble that of an alterative in that it seems to stimulate and improve the body fluids, probably through the capillary and lymphatic circulations. While in some cases the effects may be reasonably prompt, in others the changes may be gradual and a long course of treatment be required.

Echinacea, while sometimes producing rapid and brilliant results, may, in other instances, be found wanting. Its variability in quality and its use for conditions in which it is not indicated may account for some of its failures. It would seem, however, from the evidence at hand, that with conservative use and due regard to failure as well as success, that echinacea should be a valuable addition to veterinary therapeutics.

THE DIGESTIVE ACTION OF BILE IN SOME DOMESTIC ANIMALS.*

A PRELIMINARY REPORT.

O. P. JOHNSTON.

The liver is one of the largest organs of the body, and its external secretion—the bile—is one of the most copious secretions of any of the organs. The functions of the bile have been studied and discussed as widely—perhaps more widely—than those of almost any other secretion. And yet at the present time there is probably not another secretion concerning the functions of which there is less unanimity of opinion among eminent writers on the subjects of physiology and physiological chemistry. Almost every function in digestion has been ascribed to it, and every one has been disputed, and seemingly by equally eminent writers. To quote from a few text books of the present time :

"STEWART'S MANUAL OF PHYSIOLOGY." (3rd Edition.)

"* * * * * * The great action of the bile in digestion is undoubtedly the preparation of the fats for absorption, either in the form of a mechanical suspension or emulsion, or in solution as soaps ; and this it accomplishes not by itself, but in conjunction with the pancreatic juice. * * * * * * In bile * * * there is no fat splitting ferment, and according to the best experiments bile alone has no emulsifying power. But we now come to a remarkable fact : this inert bile when added to pancreatic juice greatly intensifies its emulsifying action, and a solution of bile salts has much the same effect as bile itself. * * * * * * Bile has been credited with a physical power of aiding the passage of fats through membranes, and it has been inferred that this has an important bearing on the absorption of fat from the intestine. But the inference does

*This work was carried on in the Laboratory of Veterinary Physiology and Pharmacology, N. Y. State Veterinary College, Ithaca, N. Y.

not follow from the statement, and the statement has been itself denied. * * * * * * Although bile has sometimes a feebly amylolytic action, this is not to be included among its specific powers, for a diastatic ferment in small quantities is widely diffused in the body."

"AMERICAN TEXT BOOK OF PHYSIOLOGY." (1900)

"Bile is of importance as an excretion in that it removes from the body waste products of metabolism such as cholesterin, lecithin, and bile pigments. * * * * * * As a digestive secretion the most important function attributed to the bile is the part it takes in the digestion of fats. In the first place it aids in the splitting of a part of the neutral fats and the subsequent emulsification of the remainder. More than this bile aids materially in the absorption of the digested fats. * * * * * * It was formerly believed that bile is also of great importance in restraining the processes of putrefaction in the intestine. * * * * * * Bacteriological experiments made by a number of observers have shown however that bile itself has very feeble antiseptic properties, as is indicated by the fact that it putrefies readily. The free bile acids and cholalic acid do have a direct retarding effect upon putrefaction outside the body ; but this action is not very pronounced, and has not been demonstrated satisfactorily for bile itself. * * * * * * It has been suggested, for instance, that the deficient absorption of fat that follows upon the removal of the bile results in the proteid and carbohydrate material becoming coated with an insoluble layer of fat, so that the penetration of the digestive enzymes is retarded, and greater opportunity is given for the action of bacteria. We may conclude, therefore, that while there does not seem to be sufficient warrant at present for believing that the bile exerts a direct antiseptic action upon the intestinal contents, nevertheless, its presence limits in some way the extent of putrefaction. Lastly, bile takes a direct part in suspending or destroying peptic digestion in the acid chyme forced from the stomach into the duodenum."

"HAMMERSTEN'S PHYSIOLOGICAL CHEMISTRY." (3rd Edition.)

"The bile, especially dog bile, has according to Moore and Rockwood, the property of dissolving fatty acids to a rather high degree, and hence it can perhaps accelerate the absorption of fatty acids split off by pancreatic juice. It is, however, without doubt, of greater importance that the bile, as Necki and Rockford have shown, facilitates the fat splitting action of the pancreatic juice. * * * * * * A specially strong preventive action on putrefaction has been ascribed for a long time to the bile. This anti-putrid action is not due to neutral or faintly alkaline bile which itself easily putrefies, but to the free bile acids, especially taurocholic acid. There is no question that the free bile acids have a strong preventive action on putrefaction outside the organism and it is therefore difficult to deny such action in the intestine. Notwithstanding this the antiputrid action of the bile in the intestine is contradicted by certain investigators. (Voit, Rohmann, Hirschler, and Terray.) Mosse has recently given further proof as to the inability of neutral bile in preventing putrefaction. He claims on the contrary that it has a temporal retarding action on the development of bacteria. * * * * * * The accumulation of fats in the intestine only renders the action of the digestive juices on proteids more difficult, and these last increase the amount of putrefaction. This explains the appearance of fetid feces, whose pale color is not due to a lack of bile pigments, but to a surplus of fat. * * * * * * As with this diet (i. e. an absence of fat in the food) the putrefaction in the intestine is no greater than under normal conditions, even though the bile is absent, it would seem that the bile in the intestine exercises no preventive action on putrefaction."

"SIMON'S PHYSIOLOGICAL CHEMISTRY." (1901)

"Formerly it was generally supposed that the bile played an important part in the progress of digestion, and was further capable of controlling the intensity of the putrefactive and fermentative processes which even normally take place in the lower intestinal tract.

It has now been definitely established, however, that aside from its emulsifying action upon fats, the secretion possesses no digestive properties whatever, and is likewise without effect upon the bacteria which are normally found in the intestinal canal. * * * * * * The bile in reality represents a most important excretory product of the animal body and may in this sense be compared to the urine. It appears that those waste products which are markedly toxic in action, and could not be carried to the kidneys through the blood current without seriously disturbing the general health, are formed in the liver directly, and are hence removed through separate channels in the bile. Substances are further eliminated in this manner which, like cholesterin, are insoluble in water, and could hence not be excreted by the kidneys."

Simon speaks of the greater putrefaction taking place in the absence of bile in the intestine and says:—"This is, however, not owing to the absence of the bile *per se* but to the fact that the unabsorbed fats envelop the albuminous material and thus prevent its further digestion, so that in the lower portion of the digestive canal, where the putrefactive processes are most intense, the bacteria find an increased amount of pabulum at their disposal, and an increase of the putrefactive processes accordingly results."

Among other functions accredited to bile, not mentioned by the foregoing authors, are the increasing of peristalsis in the intestine and limiting putrefaction by hastening the expulsion of the intestinal contents; the power to aid the pancreatic juice in the digestion of proteids; and the power to digest starch and the carbohydrates.

The above represents, I think, a fair example of the divergence of opinion to be found in almost any miscellaneous collection of so called standard text-books published within the last few years. The original articles on the subject will be referred to in a later report. In order to clear up as far as possible, at least in the writer's own mind, the cause of this confusion, and to throw any new light possible upon the subject the following work was begun.

Bile from the dog, cat, pig, cow, sheep, rabbit, and man was

used in the course of the experiments, extending over about eighteen months, and including something over two hundred samples of bile in all. The first work attempted was to determine whether bile had any appreciable digestive action on starch.

Fresh and old bile and sterile bile was added in varying amounts to starch solution (1 of bile to 1 of starch solution up to 1 of bile to 10 of starch solution) and the mixture incubated at 38° C. The starch solution used was uniformly a 1 per cent solution unfiltered, and each new solution prepared was tested and shown to be free from dextrin and the power to reduce Fehling's solution. The bile was also tested and shown to be unable to reduce Fehling's solution or to give the dextrin test with iodine. Many samples of bile did reduce Fehling's solution slightly when fresh, but such are not included in the following experiments. Such samples after standing twenty-four to forty-eight hours would usually lose the power to reduce Fehling's solution.

In testing for dextrin, starch and other interfering substances were precipitated by saturating with ammonium sulphate, and the filtrate diluted and tested with iodine. In every experiment throughout the work parallel blank tests were made with every varying condition of the experiments and hence possible error arising from methods, detected and eliminated.

The following tubes were incubated in the first series. Dog bile was used.

1. Bile + starch solution (in the proportion of 1 — 1 up to 1 — 10).
2. Bile alone.
3. Starch solution alone.
4. Each of the above acidified with hydrochloric acid.
5. Same as (4) but acidified with acetic acid.
6. Same as (4) but acidified with lactic acid.
7. Same as (4) but rendered alkaline with sod. carbonate.
8. Tubes of all above *not* incubated but left at room temperature about 15° C.
9. Bile *boiled* and starch as above.
10. Bile two weeks old (putrefying) and starch as above.

The degree of acidity and alkalinity in the above tubes was just sufficient to readily turn litmus paper. The tubes were incu-

bated over night, i.e., about twelve hours, and tests made in the morning. Results were obtained as follows :

1. Starch had disappeared—reducing substances present—dextrin slight and only present in tubes containing smallest amount of bile.
2. No change.
3. No change.
4. (1) Similar to 1. 4 (2) and 4 (3) No change.
5, 6, 7, & 8. Gave same results as 4 except that dextrin was present in alkaline tube.
9. No change.
10. No change.

Similar series of tubes were then incubated for shorter periods, one to six hours, with the same general results except that erythrodextrin appeared very early and later disappeared, and that the reduction tests appeared early and increased in intensity with longer incubation. In (8) the change was somewhat slower, as also appeared to be true of the acidified tubes, and possibly also the alkaline tubes. The time at which all starch disappeared varied from thirty minutes to several hours, or five or six hours even, depending on the proportion of bile to starch solution and also seemed to vary somewhat with different samples of bile. No exact and careful observations were made here on this point, and the bile and starch solutions were mixed cold and placed in the incubator cold. In only one sample from the whole number in the entire work was no action present after twelve hours. That was a sample of pig bile given below. In almost all cases the bile would cause several times its volume of starch solution to disappear within that time, usually in much less time.

Essentially similar series were carried through with the bile of the other animals with similar results. Some variations in the rapidity of the action of the different samples of bile was apparent from time to time as above stated, but sufficient observations on this point had not been made at the time the work was suspended, to draw any conclusions as to the constancy of the *rate* of activity of the bile. No constant variation in the bile from different animals was noted except in case of that of the pig, which seemed

somewhat slower in its power to change starch than that of the other animals tested. However, the bile from only twelve pigs was tested. These pigs were all from the same herd, reared under the same conditions, and fattened for slaughter ; so this may or may not mean that the bile of this animal is less active than that of others.

In tubes rendered alkaline the change to erythrodextrin did not seem to be retarded to any noticeable extent, but its further change seemed to be decidedly retarded when .5 per cent. or more alkali was present. The hydrochloric acid seemed to retard the action more than the acetic or lactic acids. In general, the change did not appear to be increased by the addition of appreciable quantities of either acids or alkalies to the normal bile. The degree of alkalinity of the normal bile was not determined, nor was the determination of the rate of change under varying conditions of acidity and alkalinity any more than just begun when the work was interrupted. A few data from which the above statements were made may be of interest. Ox bile was used in this series.

1. Bile + starch solution (1 — 1) + acetic acid to .1%
2. Bile + starch solution (1 — 1) + acetic acid to .5%
3. Bile + starch solution (1 — 1) + lactic acid to .1%
4. Bile + starch solution (1 — 1) + lactic acid to .5%
5. Bile + starch solution (1 — 1) + hydrochloric acid to .1%
6. Bile + starch solution (1 — 1) + sod. carbonate to .1%
7. Bile + starch solution (1 — 1) + sod. carbonate to .5%
8. Bile + starch solution (1 — 1) + sod. carbonate to 1.%.

The above tubes were incubated for twelve hours at 38° C.

Results :—

1. No starch — reduction.
2. Starch — reduction.
3. No starch — reduction.
4. Starch — no reduction.
5. Starch — no reduction.
6. No starch — reduction.
7. No starch — dextrin — no reduction.
8. No starch — dextrin — no reduction.

Dextrin was not tested for in (2), (4) and (5) where starch would obscure the direct test. In (1), (3) and (6) no red color was given with iodine. Thus it is noticed; (a) That lactic acid and acetic acid and sodium carbonate each to .1 per cent. allowed all the starch to be changed past the erythrodextrin stage and a reducing substance to appear instead. Whether this change was slower than without the acid or alkali was not determined. (b) That when .5 per cent. acetic or lactic acid was present the starch did not disappear and a reducing substance was not produced. (c) That the starch did not disappear and no reducing substance was produced in the presence of .1 per cent. of hydrochloric acid. As no test was made for dextrin in these three tubes (b) and (c) it cannot be stated whether all activity was inhibited or not. (d) That the starch did completely disappear in the presence of .5 per cent. and also 1 per cent. sodium carbonate, and dextrin appeared instead, but that no reducing substance was formed. It will be noticed that the proportion of bile and starch solution above was 1—1 which makes the fact of those showing starch still more prominent, as ordinarily several times that amount of starch would have entirely disappeared.

In only a few samples of bile was an attempt made to carefully determine the exact rate of activity. The only samples carefully observed were ox-bile and sheep-bile. The results obtained in these two were quite similar, the sheep bile being perhaps slightly more active. The bile and starch solution were raised to 38° C. separately and then mixed in varying proportions, the exact time of mixing being noted. With bile and starch solution in the proportion of 1—10 the starch had completely disappeared in two minutes in one case, and a decided reduction was obtained in one minute after mixing. Those given below were the only samples where a careful test was made in this way, so it cannot be stated whether these represent exceptional or common cases. A number of other cases of cat, dog, ox, and sheep bile in the course of this work were roughly observed to completely change from one to ten times its volume of starch in from thirty minutes to one hour when mixed at room temperature. Number V. of the series below shows a retard-

ing effect of higher temperatures on the activity of bile. The exact temperature at which all action was stopped was not determined, but in every case boiling the bile was observed to completely destroy its activity. It will also be observed that the bile used in number V. below had been kept frozen, so that a freezing temperature does not destroy its activity.

I. Bile from lamb 6–8 weeks of age.

(a) BILE + STARCH SOLUTION (1 — 1) 38° C.

5 min. — no starch.

(b) BILE + STARCH SOLUTION (1 — 5)

3 min. — no starch.

5 min. — reduction.

(c) BILE + STARCH SOLUTION (1 — 2)

1 min. — no starch — no dextrin — reduction

(d) BILE + STARCH SOLUTION (1 — 5)

1 min. — no starch — dextrin — reduction

(e) BILE + STARCH SOLUTION (1 — 10)

1 min. — starch — dextrin — reduction

2 min. — no starch — dextrin — reduction.

II. Ox bile.

(a) BILE + STARCH SOLUTION (1 — 1)

2 min. — no starch.

6 min. — no dextrin — reduction

(b) BILE + STARCH SOLUTION (1 — 5)

5 min. — starch present.

10 min. — no starch.

III. Ox bile.

(a) BILE + STARCH SOLUTION (1 — 1)

2 min. — no starch.

3 min. — reduction.

(b) BILE + STARCH SOLUTION (1 — 5)

5 min. — no starch.

6 min. reduction.

IV. Ox bile.

(a) BILE + STARCH SOLUTION (1 — 1)

3 min. — no starch — dextrin

5 min. — dextrin — reduction.

10 min. — no dextrin — reduction.

(b) BILE + STARCH SOLUTION (1 — 3)

1 min. — no starch — dextrin.

(c) BILE + STARCH SOLUTION (1 — 5)

2 min. — no starch — dextrin.

3 min. — reduction.

10 min. — no dextrin.

(d) BILE + STARCH SOLUTION (1 — 2)

1 min. — reduction.

V. Sheep bile. Bile one week old — kept frozen.

(a) BILE + STARCH SOLUTION (1 — 5) Kept at 40° C. for 5 min. before mixing.

3 min. — no starch — dextrin — reduction.

10 min. — no dextrin.

(b) Kept at 51° C. for 5 min. before mixing.

BILE + STARCH SOLUTION (1 — 1)

3 min. — starch present.

5 min. — starch present.

8 min. — no starch.

(c) Kept at 60° C. for 5 min. before mixing.

BILE STARCH SOLUTION (1 — 1)

5 min. — starch present.

6 min. — some reduction.

8 min. — some starch still present.

15 min. — no starch.

The presence of a diastatic enzyme might be suggested by the effects of temperature on the activity of bile, and by the following: Different samples of bile were precipitated with about five volumes of alcohol and let stand for twenty-four hours, the precipitate filtered off, washed with alcohol, and extracted for a short time—fifteen to thirty minutes—with a volume of water equal to the bile used. The clear, filtered extract was then incubated with starch solution. In every case the starch disappeared and dextrin and a reducing substance was formed.

Following is one case in which ox bile was used.

EXTRACT + STARCH SOLUTION (1 — 1)

5 min. — starch present — no reduction.

10 min. — starch present — no reduction.

15 min. — no starch — dextrin — no reduction.

20 min. — reduction

In other cases the action was slower but complete. The presence of various antiseptics such as an alcoholic solution of thymol, chloroform, carbolic acid .25 per cent., formalin .1 per cent., or alcohol 12 per cent. did not stop the activity of bile or the above extract, in its power to act on starch.

As to the nature of the reducing substance formed, it was found to give abundant crystals with phenylhydrazine hydrochlorate and sodium acetate, and to readily ferment with yeast giving carbon dioxide. On making a quantitative determination with Fehling's solution, then heating another portion with hydrochloric acid, neutralizing, and again making a quantitative determination with Fehling's solution, the latter determination was always a little greater than the first, but not nearly twice as great, making it probable that both maltose and glucose are produced by the digestive activity of bile. No systematic work was done to determine the relative proportions of the two at different stages of the digestion, nor to further identify the character of either.

The effect of bile on artificial pancreatic digestion of starch is quite striking. The activity of the pancreatic extract and the bile was tested separately and each diluted till its action was quite slow. The amount of starch that would be digested in a given time by the pancreatic juice alone, would be digested in one-fifth to one-tenth that time if about the same amount of bile was added as pancreatic extract used. This was true in both neutral and alkaline reactions. The results with an acid reaction was not determined. Following is one series of experiments showing this increased activity in the presence of bile. In each case the first test made on tube 1 containing the bile showed the complete disappearance of the starch, so that the exact time was probably something less than that indicated by the figures given.

A normal healthy dog was killed, the pancreas chopped up finely and extracted for ten hours with 75 or 80 cc of water. Bile from the same dog was used in these experiments. Both the bile and the above extract were diluted.

BILE + STARCH SOLUTION (1 — 5)

45 min. — starch present.

(a) PANCREATIC EXTRACT + STARCH SOLUTION (1 — 10)

Thoroughly mixed and divided into two equal parts.

To part 1, bile was added (same amount as extract present).

To part 2, no bile was added.

Two tubes placed in water bath together.

TUBE 1

3 min. — no starch — very slight dextrin.

TUBE 2

12 min. — starch present.

16 min. — no starch — very strong dextrin.

24 min. — dextrin test similar to tube 1.

(b) PANCREATIC EXTRACT + STARCH SOLUTION (1 — 20)

Thoroughly mixed and divided into two equal parts.

To part 1, bile was added (½ as much as extract present).

To part 2, no bile was added.

Two tubes placed in water bath together.

TUBE 1

6 min. — no starch — no dextrin.

TUBE 2

20 min. — starch.

25 min. — starch.

30 min. — starch.

35 min. — no starch — strong dextrin.

(c) PANCREATIC EXTRACT + STARCH SOLUTION (1 — 40)

Thoroughly mixed and divided into two equal parts.

To part 1, bile added (equal in amount to extract present).

To part 2, no bile added.

Placed in water-bath together.

TUBE 1

2 min. — no starch.

TUBE 2

15 min. — starch present.

20 min. — starch.

25 min. — starch.

30 min. — starch (trace).

As to the effect of the presence of bile on bacteria it may be said to inhibit for a time the growth and multiplication of the bacteria normally found in the intestinal tract, and to limit for a cor-

responding time their activity, practically preventing for the first eighteen to twenty-four hours the formation of gas. Work in this line was not completed, but the results obtained seemed to indicate those two facts quite clearly. In this series dog and cat bile was used for the most part, as they could be procured under aseptic precaution more easily than the others. Sterile bile only was used in this part of the work. The bile of healthy animals was in most cases sterile when taken immediately on or just before the death of the animal, and under aseptic precautions. In growing the cultures for plating the following media were used.

(1) Bouillon, — inoculated.
(2) Bouillon + bile, — inoculated.
(3) Bouillon + bile, not inoculated.

In inoculating the tubes precautions were taken to inoculate all under exactly the same conditions, from the same culture, with the same platinum loop and with a single drop of the culture only.

The difference in growth in tubes 1 and 2 was always plainly evident within six to twenty-four hours, tube 1 being always *very* decidedly more cloudy than tube 2. After incubating for varying lengths of time the three tubes were plated exactly alike, and under the same conditions throughout. After incubating for several hours or a day three plates in series would be made from each tube, plate 1 being inoculated by a single loopful from the culture; plate 2 by two loopfuls from plate 1; and plate 3 by three loopfuls from plate 2, thus reducing the number of colonies in plates 2 or 3 low enough to be easily counted. In such plating precautions were taken to have the contents for each plate thoroughly mixed before inoculating the the next plate from it, and also precautions were taken to have exactly the same amount of media in each plate, 10 cc being the amount used. All plate inoculations were of course made from the tube before pouring. Gelatin and agar media were used in plating.

In determining the effect on gas production, glucose bouillon was used for the most part, a few comparative tests being made with lactose and saccharose bouillons. The results were similar in

all three. The bouillon contained 1 per cent. of the sugar, 1 per cent. of peptone and ½ per cent. of sodium chloride.

Pure cultures of B. coli. communis, B. lactis æroginis, and mixed culture taken from the intestine of the calf and dog were used in this series.

The writer recognizes that the above methods were crude and unsatisfactory in many ways, but from the fact that in not a single case was the order of the results different from the following examples, although several hundred observations were made, it would seem that the results are not entirely without value.

On bacterial growth and multiplication.

A. Tube I. Bouillon, inoculated with B. coli. com.
Tube II. Bouillon + Bile, inoculated with B. coli. com.
Tube III. Bouillon + Bile; not inoculated.

Tubes I, II, and III incubated 6 hours, and then plated.

		Plate 1	Plate 2	Plate 3
(a)	Tube I.	not counted	3,000 colonies	17 colonies
	Tube II.	not counted	14 colonies	0 colonies
	Tube III.	0 colonies	0 colonies	0 colonies
(b)	Tube I.	not counted	253 colonies	1 colony
	Tube II.	not counted	8 colonies	0 colony
	Tube III.	0 colonies	0 colonies	0 colony

The colonies of plate 1, from tubes I and II were not counted, the number being too great but those from tube I were always *very* much more numerous than those from tube II. (a) and (b) are taken from different series of experiments in which the time of incubation was the same.

B. Inoculated tubes similar to I, II and III as above but with the mixed cultures. Incubated tubes 1 hour.

		Plate 1	Plate 2	Plate 3
(a)	Tube I.	325 colonies	not made	not made
	Tube II.	276 colonies	not made	not made
	Tube III.	0 colonies	not made	not made
		Plate 1	Plate 2	Plate 3
(b)	Tube I.	276 colonies	not made	not made
	Tube II.	130 colonies	not made	not made
	Tube III.	0 colonies	not made	not made

Similar Tubes I, II and III incubated 2 hours and then plated.

		Plate 1	Plate 2	Plate 3
(a)	Tube I.	910 colonies	not made	not made
	Tube II.	425 colonies	not made	not made
	Tube III.	0 colonies	not made	not made
(b)	Tube I.	445	not made	not made
	Tube II.	215	not made	not made
	Tube III.	0	not made	not made

Tubes similar to I, II and III as above incubated 24 hours plated.

		Plate 1	Plate 2	Plate 3
(a)	Tube I.	not counted	not counted	182 colonies
	Tube II.	not counred	not counted	90 colonies
	Tube III.	0 colonies	0 colonies	0 colonies
(b)	Tube I.	not counted	not counted	157 colonies
	Tube II.	not counted	not counted	120 colonies
	Tube III.	0 colonies	0 colonies	0 colonies
(c)	Tube I.	not counted	not counted	182 colonies
	Tube II.	not counted	not counted	117 colonies
	Tube III.	0 colonies	0 colonies	0 colonies

This series under B represents the least difference in the number of colonies in plates from I and II of any plates counted. The greatest difference appeared always in tubes incubated from 6 to 12 hours.

On gas production.

C

6:00 P. M.

1. Glucose bouillon, inoculated with B. coli. com.
2. Glucose bouillon + bile, inoculated with B. coli. com.
3. Glucose bouillon, inoculated with B. lactis aerog.
4. Glucose bouillon + bile, inoculated with B. lactis aerog.
5. Glucose bouillon + bile, not inoculated.

8:30 A. M.

1. 1 cc gas
2. No gas.
3. 4 cc gas
4. Small bubble gas only.
5. No gas.

11:00 A. M.

2. No gas
4. No change

4. That both the above activities of bile are present under the same conditions of reaction as that found in the small intestine ; i. e. varying from slightly alkaline to neutral or slightly acid with organic acids. (The effect of bile on pancreatic digestion, as above stated, was not determined for an acid medium.)

5. That the intermediate and end products formed by the activity of bile on starch appear to be dextrins, maltose and glucose as in pancreatic digestion.

6. That there is probably a diastatic ferment present in bile.

7. That bile inhibits for a time to quite a marked extent the multiplication of the bacteria normally found in the intestinal canal ; and that it materially retards the formation of gas by bacterial activity, essentially preventing it for the first twelve to eighteen hours. And it is only natural to assume that in all probability other evidences of bacterial activity as putrefaction, etc., are correspondingly retarded by its presence.

I am greatly indebted to Dr. P. A. Fish for the many ideas and suggestions freely given in carrying out this work and for the laboratory facilities and accommodations at my disposal. I also wish to express my thanks to Dr. V. A. Moore and the instructors in bacteriology for courtesies extended in that department.

[From American Veterinary Review March, 1904.]

CALCIUM SULPHIDE IN THE TREATMENT OF POLL-EVIL AND FISTULOUS WITHERS.*

BY BERT RAYMOND WILBUR, D.V.M., RANDOLPH, N. Y.

Calcium sulphide or sulphuretted lime is a pale gray powder, exhaling a strong odor of hydrogen sulphide, and having an offensive alkaline taste and reaction. It is insoluble in alcohol, very slightly soluble in cold water, and is decomposed by boiling water.

As the salt readily deteriorates and decomposes from exposure to air, it should be kept in tightly sealed containers and should not, therefore, be dispensed in the form of powders with the expectation of obtaining complete and satisfactory results.

In 1869 Dr. Ringer claimed for the sulphides, and for this preparation particularly, the power of arresting suppuration. He recommended the use of one grain of calcium sulphide in eight ounces of water and a teaspoonful of the solution to be taken every hour. To this was ascribed the cure of scrofulous and tuberculous abscesses in human practice.

Its use in human medicine is very extensive and seems to have found considerable favor. It has been described as the best anti-suppurant known, where the condition is not due to syphilis. The mucous membranes being influenced by it and suppurative action checked, as in the early purulent stages of bronchitis and pneumonia, also in nasal catarrh where the secretion is abundant with a tendency toward purulency. As a remedy for successive crops of boils, it is said no agent is superior.

The influence of calcium sulphide, on the suppurative process, is described by Dr. Ringer as follows: "A thin, watery, unhealthful discharge becomes, at first, more abundant, then diminishes and becomes thicker and healthier, like 'laudable pus'; the condition of the sore improving correspondingly, its healing, the while, being promoted. In some cases, any pain that exists is temporarily

*Abstract of a Thesis presented for the degree D.V.M., at the New York State Veterinary College, Ithaca, N. Y., June, 1903.

aggravated, but as a rule, it is speedily mitigated. The general health improves and the debility and feeling of uneasiness and discomfort, so frequently attending these maladies, promptly passes away."

According to Shaller, "the drug is decomposed in the body, the sulphate of calcium passing out in the fæces, and the sulphuretted hydrogen after absorption into the blood is eliminated by the skin and lungs. Because of this elimination by the lungs, this drug produces excellent results in diseases of the bronchial tubes, where the sputum is scanty and tough and where the cough is distressing."

So far as I have been able to find, there are no recorded cases of its use in English veterinary literature, except a few cases recorded in Dr. Law's work on Veterinary Medicine. It is recommended in this work, in cases of purulent nephritis and in inflammation of the renal pelvis. Dr. Law gives one case of an old quittor where its administration internally effected a speedy cure. He also recommends it in cases of furunculosis or boils occurring on the digital regions of horses in winter, or where the parts are exposed to street mud containing an abundance of decomposing organic material. In these cases the sulphide was given internally combined with local applications of phenol or tincture of iodine.

The use of calcium sulphide in this research was confined to the treatment of poll-evil and fistulous withers only. In all, seventeen subjects were experimented upon, a few of these (four or five) were not suffering from acute disease but were experimented upon to determine the proper physiological dosage. Doses ranging from five grains to two ounces were tried with varying results. Many of the diseased cases were not under my complete control and received other internal treatment which, within certain limits, rendered the sulphide treatment unreliable. Therapeutic doses have no marked effect upon the pulse, respiration and temperature.

Case one, patient, a black mare weighing about 1050 pounds. When brought to the clinic there was a fistula on the side of the withers discharging quite freely. The tract was laid open freely and continuous irrigation kept up for several days, in order to

allay the inflammation and to get disinfection. After a week the administration of the sulphide was begun, two drachms being given three times a day. Later on, an ounce dose daily was given and still later a two ounce dose daily was administered. The discharge from the wound was quite excessive and a new pocket of pus had developed. The patient ate well while receiving the large doses and the general health did not seem to be affected. The sulphide was also applied locally to the wound, but this seemed to increase the discharge. The medicine was withheld for a week and then resumed in ounce doses. Another pocket of pus had developed in the meantime and this was opened and thoroughly cleaned. Some days later there was still quite a free discharge but the wound was healing slowly. The patient was under observation thirty-nine days. During this time there was no very marked changes in the respiration, pulse nor temperature. The lowest number of respirations recorded were 8, the highest 18; the lowest pulse record was 38, the highest 56; the lowest temperature was 98.4°, and the highest 101.8°. These variations were due not merely to the dosage, but in part at least to a variation in the condition of the animal as a result of the disease. It was observed that no digestive disturbances appeared as a result of the large doses, which seems to be contrary to the experience in human medicine.

Cases two, three and four were of a similar character, except that they received a uniform dosage of fifteen grains of calcium sulphide three times a day. Case three was a cow and was discharged after twenty-three days, but later on was returned for further treatment. Cases two and four were horses and were under observation for thirty-seven and thirty-three days respectively. Potassium iodide was also given internally. In both of these cases it was found that the pus had burrowed a second time after the treatment had begun.

Cases five to eleven inclusive were not diseased but were used solely for experimental dosage. Three of the horses received one drachm doses of the sulphide three times daily. In one of them the temperature and pulse increased slightly above normal; in the

other two the temperature and pulse were slightly decreased. In another horse receiving one drachm once a day there was a slight rise in temperature and pulse; but in another horse receiving a half-drachm dose once daily there was a slight decrease. The two remaining horses in this series received five and fifteen grain doses respectively of the sulphide once daily. The temperature, pulse and respiration remaining within normal limits. Although an increase and decrease is referred to above, the variations from normal were very slight.

Case twelve was a sorrel mare weighing about 1000 pounds. This case was purely experimental, the aim being to produce the disease and begin treatment early in the course. Some pus was collected from a patient suffering from poll-evil. Bouillon cultures were made from the pus and 3.5 c.c. of a one-day old culture were inoculated over the region of the poll of the mare, but a little to one side of the median line. Due antiseptic precautions were taken in collecting the pus and making the inoculation. The day after the inoculation a large tender swelling appeared at the point of inoculation. The mare's appetite declined and the swelling increased in size. The neck became somewhat stiffened and there was evidence of increasing tenderness over the poll. Six days after the inoculation five grain doses of the calcium sulphide were given twice daily. The swelling remained at about the same size but there was evidence of less soreness and the patient ate freely. After five days the dose was raised to ten grains twice daily and three days later fifteen grain doses were given. There was less stiffness of the neck and no increase in the size of the swelling, although it was still quite sore. Sixteen days after the inoculation, a thin watery fluid was discharged from the swelling and a day later a thick creamy pus appeared. On examination it was found that nearly the entire surface of the swelling was necrotic and the hair upon this surface was loose and easily removed. The mare was confined in the stocks and the abcess freely opened, discharging a half pint of pus. On probing, a fistula was revealed running down the side of the neck, for a distance of five or six inches. The silver probe used in

exploring the abscess became considerably blackened, indicating the presence of sulphuretted hydrogen from the calcium sulphide which had been administered.

As much pus and necrotic tissue as possible were removed involving a total area of six or eight square inches. A ring of hair, one or two inches in width, was removed around this area, the hair coming out quite easily. After securing efficient drainage the wound was carefully disinfected and dressed with a pack soaked in a solution of lysol. Subsequent dressings consisted of injections and washings with a solution of echafolta. Internal treatment with calcium sulphide was kept up and in two weeks recovery was complete. During treatment the lowest pulse was 40 and the highest 60. The lowest temperature was 99° and the highest 103°.

Case thirteen was a control of the previous case. This subject was inocculated with the same amount of bouillon culture as case twelve. The swelling appeared the next day and the general symptoms coincided closely with those of the previous case. After two weeks the subject was killed and about half a pint of partly inspissated pus was obtained from the abscess. In neither of these two cases was the ligamentum nuchæ involved. Case thirteen received no treatment whatever. At the time of killing there was no indication of *pointing* in the abscess and the pus was less fluid than in number twelve. The inference is that the calcium sulphide, in the previous case, hastened the ripening of the abscess (which was discharging after sixteen days) and stimulated the healing process.

Cases fourteen, fifteen, sixteen and seventeen were regular patients at the clinic and received ten grain doses of calcium sulphide twice daily, except number fifteen, which received a twenty grain dose once a day. This patient also received potassium iodide internally. Two of these cases had received previous treatment outside of the clinic, without success, but yielded readily to the combined local and internal treatment. Case seventeen was under observation one week, but was sent home before complete recovery with directions to the owner as to proper treatment. This was not carried out and the patient was returned later in poor con-

dition and with new pockets of pus forming. The calcium sulphide had been administered but the local treatment had been neglected. This case is cited to emphasize the desirability of maintaining good local treatment. The evidence is that the quickest results may be obtained by the proper combination of the two.

As a summary of the observations taken during this work it would appear: 1. Doses of calcium sulphide larger than ten or fifteen grains twice daily tend to increase the discharge and perhaps hinder the healing process. 2. Large doses disturb the temperature and pulse. 3. Large doses, even as high as two ounces daily, do not appear to cause derangement of the digestive system in the horse. 4. Calcium sulphide locally applied increases the discharge. 5. The best effects are obtained when calcium sulphide is used without the administration of other drugs. 6. The administration of small doses of the sulphide (10 grains) appears to lessen the discharge and prevent the burrowing of the pus. 7. Good local treatment is essential, by freely opening the fistulæ and keeping the wound thoroughly disinfected. 8. A convenient method to administer the drug is in gelatin capsules of the proper size. These protect the drug from the air and will be readily taken by the horse when given with moistened feed. 9. It is best not to administer the drug until the fever caused by the operation has subsided. 10. The patients do not appear to lose condition during the treatment, but tend to increase in flesh. 11. Without a good quality of the drug, no good results can be obtained. Calcium sulphide rapidly loses its properties when exposed to the air.

Acknowledgments for advice and suggestions are due to Drs. Fish, Law, Williams and Hopkins.

THE EFFECT OF CERTAIN DRUGS UPON BLOOD PRESSURE AND CARDIAC INHIBITION IN THE HORSE.

PIERRE A. FISH, ITHACA, N. Y.

The more a man knows of his tools, the better qualified is he for his work. This truism applies with peculiar force to all who prescribe medicines. Drugs are the tools with which the physician works to assist nature in overcoming abnormal conditions in the organism. Massed personal experience and clinical evidence or therapeutics stand high in determining the value of the use of particular drugs for certain pathologic conditions. Pharmacology endeavors to supply detailed facts concerning the physiologic action of drugs, and aims to supplement clinical observations with reliable data.

In the following experiments the usual apparatus for blood pressure demonstrations was employed. In all cases the carotid artery was connected with a mercury manometer, the floater of which wrote its record upon a cylinder revolving at a uniform speed.

Data have been obtained from sixteen horses, two cows, one calf, one cat and a number of dogs; the special purpose being to note the effects of drugs upon the rate and force of the heart and its susceptibility to inhibitory stimuli transmitted through the vagus nerve. In nearly all cases the drugs were administered intravenously, the jugular vein being utilized in the larger and the femoral vein in the smaller animals. Chloroform anaesthesia was employed for the horses, cows and calf; morphine or chloretone with ether or chloroform for the dogs and cats.

In general an increase in the amount of blood pressure is due to an increased force or activity of the heart-beat, or an increased resistance or constriction of the peripheral blood vessels; the opposite conditions with regard to the heart and peripheral vessels cause a diminished pressure.

Inhibition means a diminution in the frequency of the heart-beat, or complete standstill—the heart remaning in diastole—according to the strength of the stimulus sent into the heart through the inhibitory fibers of the vagus nerve. Continued stimulation, however, does not produce continued inhibition, for after a variable limit the heart escapes from the control of the vagus and resumes its beating in spite of the stimulus. The vagus nerves also vary in their power of controlling the action of the heart; for in some cases while stim-

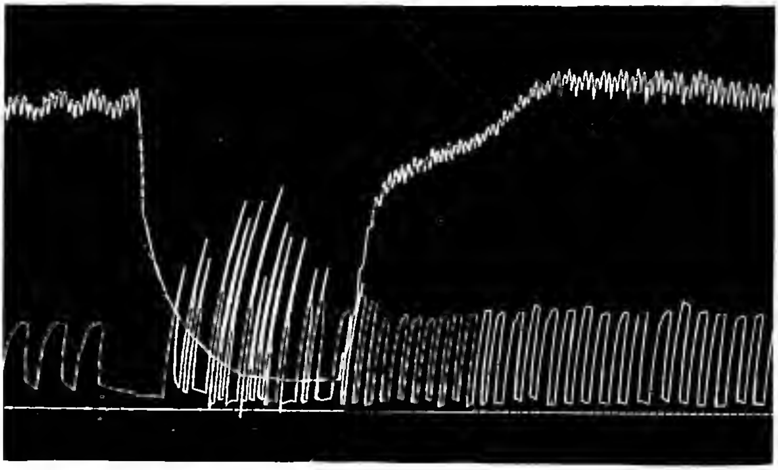


FIG. 1.—TRACINGS OF BLOOD PRESSURE AND RESPIRATION. DOG.

Effect of Vagus Stimulation. The upper tracing is of the blood pressure; the drop in the tracing occurred when the vagus nerve was stimulated. The lower tracing is of the respiration. Stimulation of the vagus had the effect of increasing the respirations. Reduced three-eighths.

ulation of the nerve on one side will inhibit the heart the same stimulus applied to the opposite vagus may actually cause acceleration. In other instances either vagus controls the heart with equal facility. The tracings represent cardiac autographs, in which the heart writes its own record, strongly or weakly as the case may be.

Fig. 1 shows complete cardiac inhibition and consequent fall in blood pressure from moderate electric stimulation of the vagus nerve. The response was not immediate, there being at

least one beat before inhibition ensued. When the stimulus was removed there was again an appreciable delay before the beating was resumed. Ultimately there was a somewhat increased rate with higher blood pressure as if to make up for the time lost during inhibition. The upstrokes in the blood pressure curves represent the systolc; the downstrokes the diastole of the heart. Upon respiration there was at first inhibition, followed almost immediately by increased depth and frequency and some irregularity in breathing. Upon the removal of the stimulus, the depth and frequency was still maintained slightly above the normal.

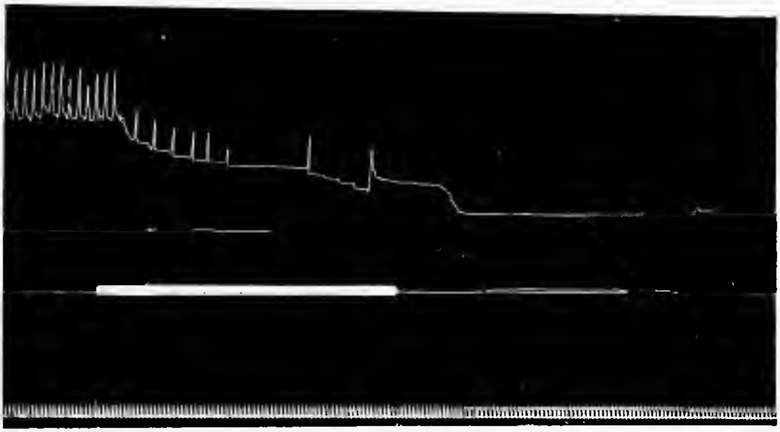


FIG. 2.—BLOOD PRESSURE TRACING. HORSE NO. 5.

Strongest Stimulus. The broad line below the tracing indicates the period of vagus excitation. The lower line marks seconds. Reduced one-half.

The tracing in Fig. 2 shows a fatal termination. Through an inadvertency the short circuiting key of the apparatus was not opened until the strongest stimulus was reached. The usual practice in the experiments was to first apply a weak stimulus and gradually lead up to the strongest. This has been done a number of times, and in such cases there has been no fatal result. As an explanation, it may be suggested that the weaker stimuli "educate" the heart to resist the vagus effect, so that it acquires to some extent an immunity against strong stimuli. Such an hypothesis, however, requires further confirmation.

It should be noted in this case that the heart showed considerable resistance to the excitation, giving three normal beats and then continuing to beat with diminished force and frequency while the blood pressure fell gradually. The stimulus was applied for seventy seconds. When this was removed the blood pressure continued to fall slightly. After about seventy seconds more the heart gave one abortive beat, when death ensued. The cylinder was allowed to revolve its whole circumference (about eighteen inches), and the floater showed a continued but almost imperceptible decrease in blood pressure.

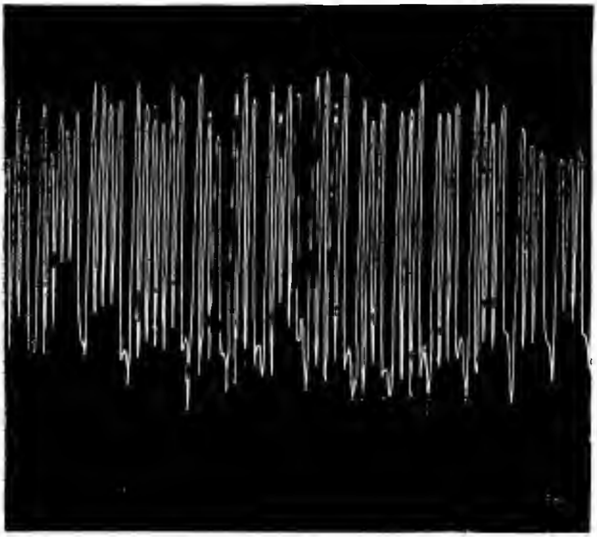


FIG. 3.—INTERMITTENT PULSE. HORSE NO. 8.
Blood Pressure Tracing. Natural size.

An abnormal condition not infrequently encountered is an intermittent and irregular pulse. The tracing shows the missing beats at more or less regular intervals and that there is usually an abortive attempt to beat, which, however, is too slight for the finger to detect.

In this experiment a single electrode was placed upon each vagus, and the stimulus sent through both nerves simultaneously Blood pressure is considerably lowered, with diminished fre-

quency but increased amplitude in the heart beat. The result is much the same as when a pair of electrodes is placed upon the single nerve.

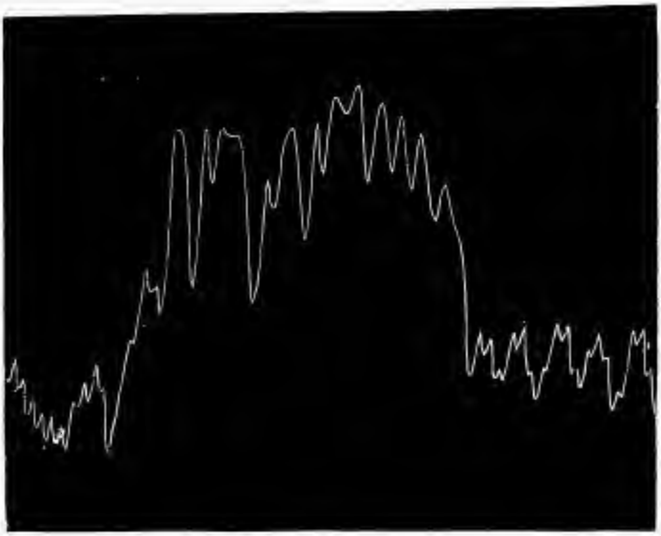


FIG. 4.—BLOOD PRESSURE TRACING. CALF NO. 1.
Moderate Stimulus to Vagus Nerve. Natural size.

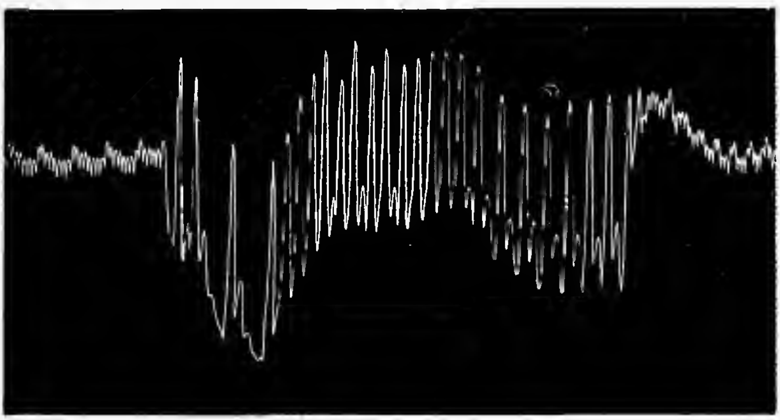


FIG. 5.—BLOOD PRESSURE TRACING. COW NO. 1.
Moderate Stimulation of Vagus Nerve. Reduced one-half.

This cow was tuberculous. The heart was slow to react to the stimulus, giving eight beats before the blood pressure

fell. The decrease in frequency is very great, but the enormous increase in the amplitude of the heart beat during the period of stimulation is remarkable. Shortly after the removal of the stimulus the blood pressure rose, but soon returned to normal.

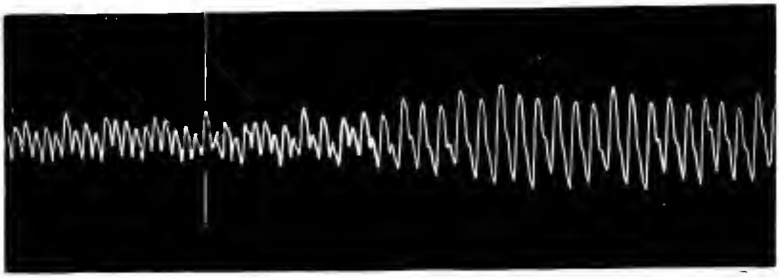


FIG. 6.—BLOOD PRESSURE TRACING. COW NO. 1.
Effect of Eserine Upon the Heart. Reduced one-eighth.

Three grains of eserine sulphate were injected into the right jugular vein at the point on the tracing indicated by the vertical line. The effect was to soon slow the action of the heart, but to increase the force of its beat. In general the

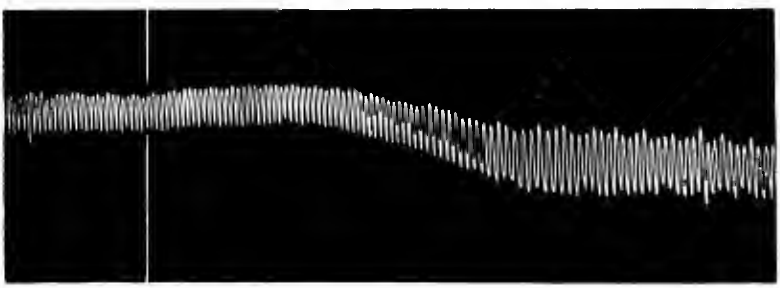


FIG. 7.—BLOOD PRESSURE TRACING. HORSE NO. 16.
Effect of Nitroglycerine Upon Blood Pressure. Reduced three-sixteenths.

force of the beat is measured by the vertical distance of each individual curve and the frequency by the horizontal distance between each curve. Eserine exerts a direct stimulating action upon the cardiac muscle independently of the vagus nerve.

One grain of nitroglycerine was injected into the left jugular vein at the point indicated on the tracing. The blood pressure fell gradually with decreased frequency but increased am-

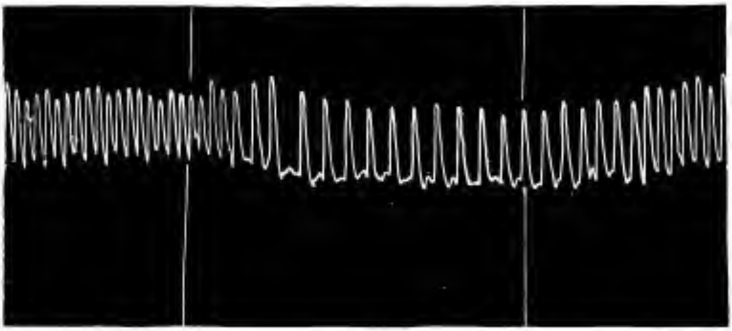


FIG. 8.—BLOOD PRESSURE TRACING. HORSE NO. 16.

Strong Stimulus Applied to the Left Vagus after the Injection of Nitroglycerine. The distance between the two sets of vertical lines shows the period of vagus stimulation.

plitude of the heart beat; this effect being brought about by the paralyzing action of the drug upon the vaso-motor mechanism. The peripheral as well as the central mechanism being affected.

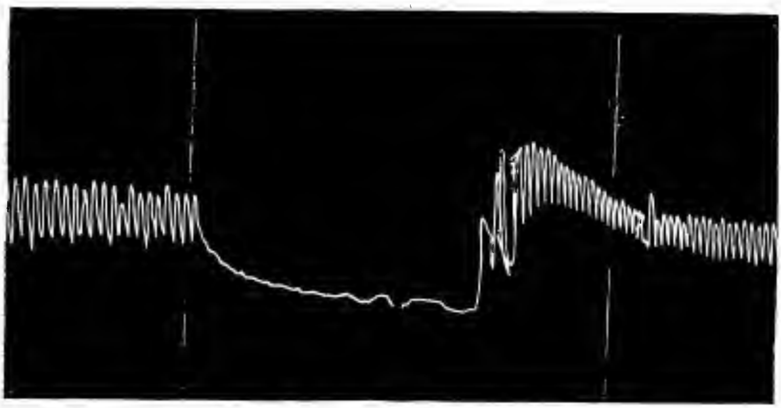


FIG. 9.—BLOOD PRESSURE TRACING. HORSE NO. 16.

Strong Stimulus to the Right Vagus after Nitroglycerine. The two sets of vertical lines indicate the period of vagus stimulation. Reduced one-sixteenth.

After the effect of the nitroglycerine was apparent a strong stimulus was applied to the vagus nerve of the left side for

twenty-eight seconds. The principal action is the slowing effect upon the rate, which was maintained for a short time after the stimulus was removed. There is a slight fall in blood pressure, the amplitude of the beat being practically the same throughout. Nitroglycerine tends to paralyze the vagus center as well as the vaso-motor, and a mild stimulus produces practically no marked effect upon the heart beat.

In this experiment the same strength of stimulus was sent into the right vagus as had just previously been sent into the left, and illustrates the difference in susceptibility of the vagus nerves in their control of the heart. Although there is a fall in blood pressure, there is not complete inhibition, as the

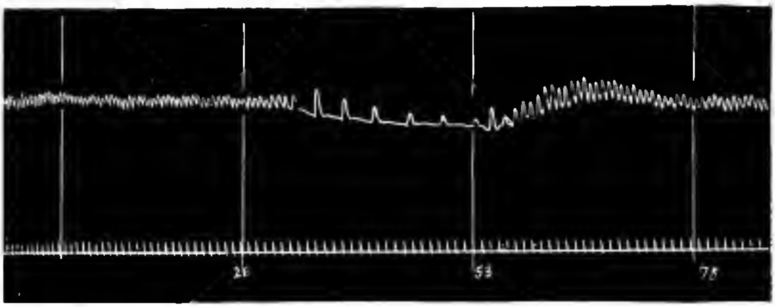


FIG. 10.—BLOOD PRESSURE TRACING. HORSE NO. 16.

Nitroglycerine Experiment: Stimulation of Both Vagi. The distance between the first and last vertical lines represents the long period of stimulation (right vagus). Between the second and third verticals, the period of short stimulation (left vagus). Reduced one-fourth.

tracing shows a number of abortive beats. The stimulus was applied for forty-three seconds, during which the heart escaped from the control of the vagus, and beat with increased force and frequency and with higher blood pressure for thirteen seconds before the removal of the stimulus.

A strong stimulus extending through a period of seventy-eight seconds was sent into the right vagus. During the first twenty-six seconds there was practically no effect upon the heart rhythm except a slight slowing in the rate. (Compare with Fig. 9.) After twenty-six seconds, while the right vagus was still being stimulated, a current of the same strength was turned into the left vagus for twenty-seven seconds. After

some delay there was a slight fall in blood pressure, with marked slowing of the heart. After the removal of the stimulus from the left vagus there was an increase in the blood pressure and increased force to the beat, in spite of the fact that the right vagus was still receiving its stimulus. The removal of all stimulation produced no apparent change in the heart beat nor in the blood pressure. The experiment was concluded by cutting both vagus nerves, without producing any material change in the character of the tracing.

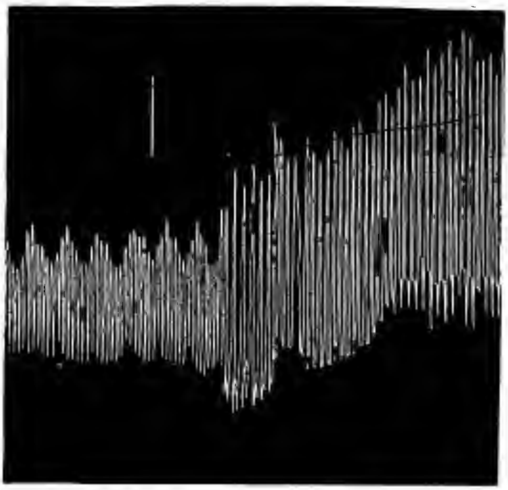


FIG. 11.—BLOOD PRESSURE TRACING. HORSE NO 6.

Normal Pressure Tracing at the Left; Effect of Barium Chloride Shown at the Right. The vertical line above the tracing indicates the point at which the barium chloride was injected. Natural size.

Ten grains of barium chloride were injected into the jugular vein, causing a very decided increase in the force of the contraction, at the same time slowing the rate of the heart. The rise in blood pressure is also striking.

The strongest stimulus was applied for one hundred and five seconds. The response was almost immediate, as shown by the sudden fall in blood pressure. The beating of the heart was checked only temporarily; the beats, though somewhat irregular and of less amplitude, were nearly as vigorous as normal, and the blood pressure rose materially in spite of the

strong and long stimulation. Upon the removal of the stimulus there was immediate recovery, as shown by the increased frequency, and some rise in blood pressure, although the latter remained lower than the normal. Barium chloride evidently interferes with the vagus control of the heart.

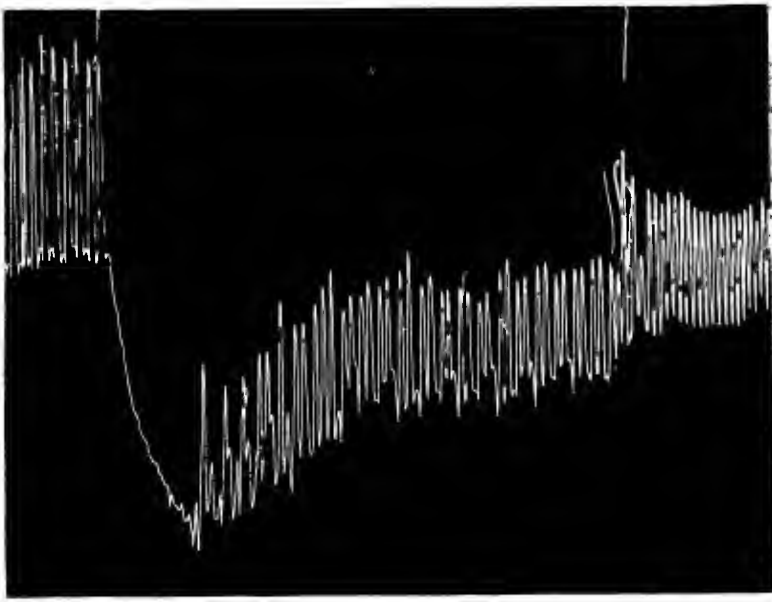


FIG. 12.—BLOOD PRESSURE TRACING. HORSE NO. 6.

Strongest Stimulus to Vagus after Barium Chloride. The vertical lines above the tracing indicate the period of vagus stimulation. Reduced one-sixteenth.

The strongest stimulus was applied to both vagus nerves for thirty-one seconds. The slow response is remarkable. There is considerable fall in blood pressure and the slowing and irregularity of the heart is marked with greatly increased amplitude in the beat, but there is not complete inhibition. The recovery from stimulation is even slower than was the response. The blood pressure rose above normal for a short time, and the frequency of the heart beat did not quite return to the original. In this experiment the barium was injected subcutaneously.

As in the preceding experiment the strongest stimulus was employed, but for a longer period (one hundred and twenty-seven seconds). There is also noted the same delay in response and recovery from the stimulation. At first there is a little irregular fall in blood pressure; but this is soon maintained at the normal, while the force of the contraction is greatly increased, but somewhat slowed. In this experiment both vagi had been cut and the stimuli were applied to the

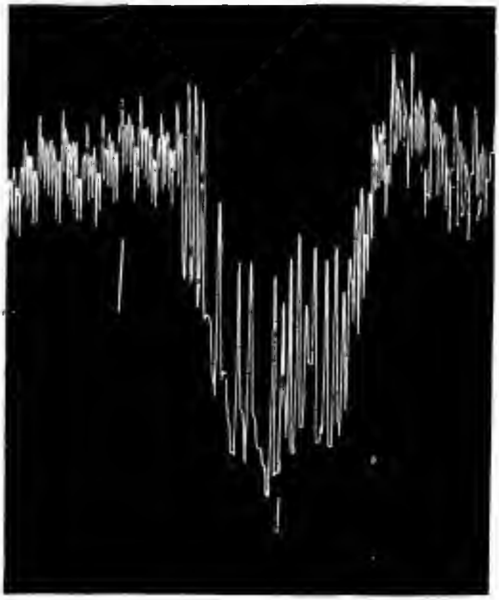


FIG. 13.—BLOOD PRESSURE TRACING. HORSE NO. 7.
Stimulation of Both Vagi after Barium Chloride. The vertical lines below the tracing show the period of vagus stimulation. Natural size.

peripheral portions of the cut nerves; the cardio-inhibitory center was therefore separated from direct connection with the heart and its influence was removed. A comparison of Figs. 13 and 14 is most interesting. In the former the vagi were intact, and the center formed a portion of the circuit; in the latter case the center was excluded, all other conditions, however, being the same. The more pronounced effect in the first case suggests that normally or under the influence of the

drug the center responds to the electric excitation, and sends inhibitory stimuli to the heart in addition to those directly transmitted by the electrodes; for in the second case, where all

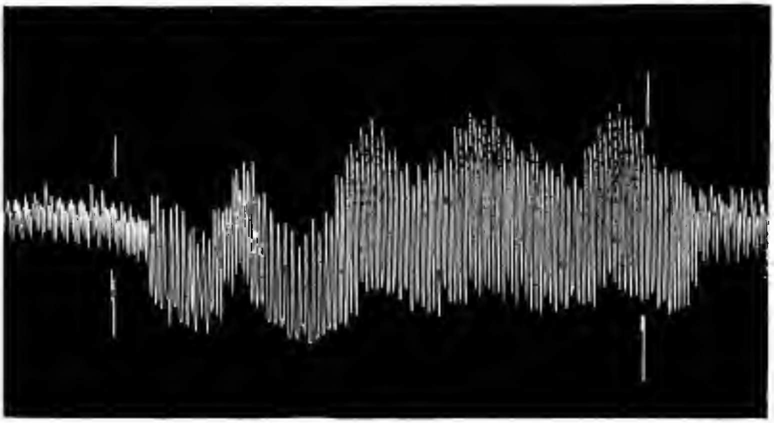


FIG. 14.—BLOOD PRESSURE TRACING. HORSE NO. 7.

Stimulation of the Peripheral Portions of the Cut Vagi after Barium Chloride. Period of vagus stimulation is shown by the vertical lines above and below the tracing. Reduced three-eighths.

of the conditions were the same except the inclusion of the center, the inhibitory effects were very much less pronounced.

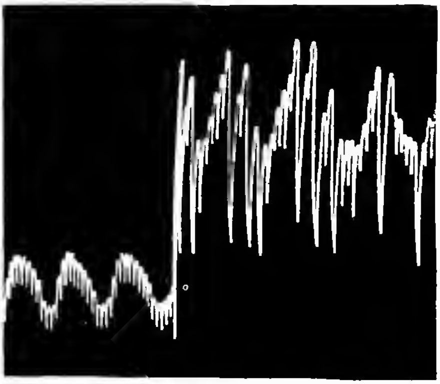


FIG. 15.—BLOOD PRESSURE TRACING. DOG.

Normal Condition at the Left and Effects of Barium Chloride at the Right. Natural size.

The question as to the acquisition of immunity by the heart from previous stimulation, if this be a fact, may also have an application here.

In this dog one-fourth of a grain of barium chloride was administered in the femoral vein. The increase in the blood

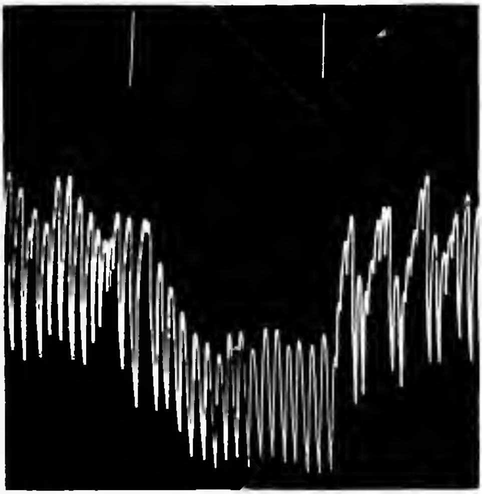


FIG. 16.—BLOOD PRESSURE TRACING. DOG.

Vagus Stimulation after Barium Chloride. The vertical lines above the tracing show the period of stimulation. Natural size.

pressure, more forcible contraction and slowing of the beat is well demonstrated.

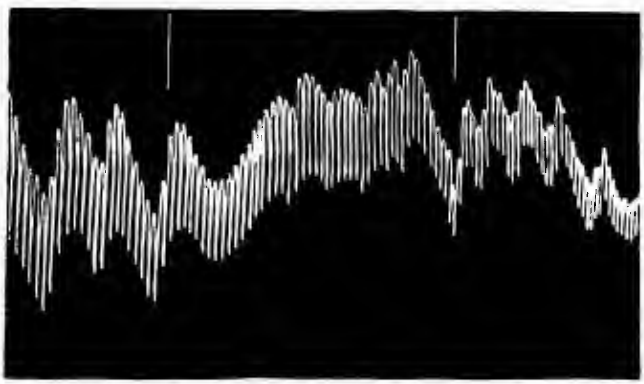


FIG. 17.—BLOOD PRESSURE TRACING. DOG.

Vagus Stimulation Between Vertical Lines after Atropine Following Barium Chloride. Natural size.

As in the case of the horse, some resistance is shown toward the vagus control of the heart. With a moderate stimu-

lus the amplitude of the beat is not much decreased, although there is a fall in blood pressure and some slowing.

The administration of atropine (same dose as barium chloride) shows an increased activity of the heart on account of the paralysis of the vagus endings. There is also an increased blood pressure, due to the greater output of blood from the heart as well as to stimulation of the vaso-motor center in the oblongata. Excitation of the vagus after atropine does not produce inhibition. In this case it caused the opposite result, producing a rise in blood pressure without any very appreciable effect upon the amplitude or frequency of the beat.

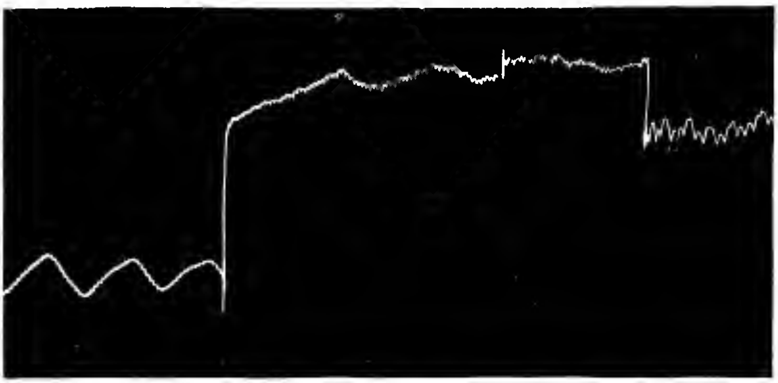


FIG. 18.—BLOOD PRESSURE TRACING. CAT.

Tracing of Normal Pressure at the Left, and after the Administration of Barium Chloride at the Right. Reduced one-half.

This cat received a very large dose of barium chloride in the femoral vein (1.7 centigrams per kilogram of body weight, or a total dose of about 5-6 grain). As shown by the tracing, the first effect of the drug was to produce vaso-constriction. The blood pressure increased in amount to seventy-six per cent above normal. In time the pressure fell a little, but was maintained at a point much higher than normal, with slowing and increased force in the contraction.

In general the tracings show an important effect of barium chloride upon the heart and circulation. The resemblance to digitalis in these respects is very marked, and is extended also to its diuretic effect. In an experiment upon a dog it

was observed that the flow of urine through the ureters and collected in a graduate exceeded the normal volume considerably in a given time. The diuretic effect of barium chloride as well as of digitalis is undoubtedly due to the action of the drugs upon the blood pressure in the kidneys.

Loeb has shown that the barium ion exercises a stimulating effect upon protoplasm, especially all forms of muscle tissue. The results of the foregoing experiments would indicate that the barium, by stimulating the cardiac muscle directly, enables it to resist, within certain limits, the vagus control.

The increase in blood pressure is effected by the vaso-constricting action of the salt, possibly by its direct action upon the muscular tissue of the vessels. The increased force of the heart beat should also be considered a factor. The slowing of the heart would indicate that barium chloride also has a stimulating effect upon the vagus mechanism.

Dr. Schedel of Nauheim, Germany (*Deut. Med. Woch.* xxix No. 13), experimenting upon himself, observed the effect of barium chloride upon the heart and circulation. After obtaining his normal pulse and blood pressure by the use of a sphygmograph and tonometer, he found that, taking one-third of a grain of the salt twice daily, two hours after the principal meals, the effects were produced two hours later. These effects were a fall in the pulse rate, an increase of 10 mm. in the blood pressure, and greater amplitude of the pulse curve. There was still some effect of the drug three days after it was discontinued.

In another experiment, where three-fourths of a grain was taken twice daily, the results were the same, except that the blood pressure increased 30 mm. in amount.

Clinically the drug was used upon nineteen patients, some suffering from organic heart disease and others with lowered blood pressure resulting from such diseases as pulmonary tuberculosis, leukemia or chlorosis. Doses of one-third grain or one-half grain, twice daily, caused considerable improvement, the pulse becoming regular, full and slower, the grave symptoms disappearing with the rise in blood pressure and free diuresis. The increased blood pressure did not last longer than three days, but the general improvement and the strengthened pulse persisted for eight days.

Dr. Schedel concludes that the indications for barium chloride are the same as those for digitalis, and that small doses do not disturb the digestive functions.

It would appear from the data already given that the veterinarian will probably find in barium chloride, with proper dosage, a valuable drug in animal therapeutics, aside from its use in producing purgation, where doses bordering upon toxicity are required.

ABSTRACTS

OF

WORK DONE IN THE LABORATORY

OF

VETERINARY PHYSIOLOGY AND
. . . . PHARMACOLOGY . . . .

UNDER THE DIRECTION OF P. A. FISH

NO. 2

NEW YORK STATE VETERINARY COLLEGE
CORNELL UNIVERSITY
ITHACA, N. Y.
1905

TABLE OF CONTENTS

THE EFFECT OF MOLASSES FEEDING ON HORSES AT REST.

P. A. FISH AND A. M. SEAMAN.

ITHACA, N. Y.

(Read at the meeting of the N. Y. State Veterinary Society, Brooklyn, Sept. 14, 1904.)

The use of molasses as a food for stock was suggested by Hermstadt as early as 1811. In Europe it has been used as a stock food for a number of years. In some countries it has been subject to taxation and its cost, therefore, has been an important factor in determining its general use. In Austro-Hungary during 1900–1901, six per cent., and in Germany 27.6 per cent. of the total product of molasses was used for feeding purposes. It has been fed largely to cattle with the idea of improving the quality of the beef and in some cases of increasing the milk production. It was found that when molasses was used, the hay and grain might be diminished and that it rendered food of poorer quality more palatable. It was fed in quantities ranging from 5 to 12½ pounds per day.

Some experiments in molasses feeding were carried on by Dr. Griffin in Porto Rico from 1898 to 1901. Thirty-five pounds of grass and 13 to 15 pounds of molasses were used as a daily ration. When beginning the new ration there was an average loss of 27 pounds in weight. This loss, however was soon made up and the animals gained over the original weight. He found that the horses did more work and presented a better appearance as a result of the molasses feed and the cost of their maintenance was reduced from 27 cents to 15 cents per day.

Dr. Liautard of Paris reports, concerning molasses peat, that there is no danger nor inconvenience in its use; that the general condition, muscular power, energy to work and the health of the animals remained perfect the coat presenting a better and more glossy appearance; that when subject to colic and indigestion, the attacks are less severe, less frequent and sometimes disappear.

In 1902 Berns experimented with molasses upon two unthrifty horses weighing 900 and 940 pounds respectively, feeding one quart of molasses diluted with three quarts of water three times a day with some grain and hay. There was no constipation nor indigestion. In six weeks horse No. 1 had gained 175 lbs. and No. 2, 146 lbs. A number of truck horses were also experimented with. All improved in condition; the general health was excellent, acute indigestion and spasmodic colic were rare although they had been frequent before the experiment.

The Colonial Sugar Co., of Fiji, Australia, also report experiments with molasses. They fed at one time as much as 30 pounds per day, but believing this too high they reduced the amount to 15 pounds per day as a steady diet, given along with 3 pounds of bran and 4 pounds of corn with as many green cane tops as the animal could eat. Some constipation was noticed and the bran was given to correct it. They concluded that an albuminoid ratio as low (wide) as 1:11.8 is suitable for heavy continuous work. (1.13 lbs. digestible albuminoid, 13.30 lbs. of carbohydrates including 0.24 lb. fat equals 1:11.8). Such a ration they believe to be suitable in a tropical climate. No undue fattening, softness or injury to wind was observed.

Grandeau's experiments showed sugar to possess a coefficient of digestibility amounting to 100, *i.e.*, all the sugar was digested, none being found in the droppings. The thirst was not increased, in fact, it was a fraction less than when sugar was not used.

Other experimenters also report quite uniformly favorable results.

As a summary of the testimony in numerous reports the following conclusions seem warranted:

Good molasses is a highly nutritive food easily digested, and assimilated, and in some cases at least corrects faulty digestion.

One quart of molasses at 3 cents will take the place of three to four quarts of good oats at 4½ to 6 cents.

The sudden change from dry oats to molasses mixed with other foodstuffs is safe and causes no marked disturbance of the digestive organs.

Molasses fed horses will do as much or more work and remain as a rule in much better general condition.

The cost of feeding, depending upon locality, may be reduced from 25 per cent to 33 per cent. In some localities there is no reduction.

In general, molasses may be considered as a product containing sugar that cannot be crystalized by any known method. Its composition is to a certain extent variable and the following would perhaps represent an average analysis :

Water	20 per cent.
Dry substances containing :	
Nitrogeneous substances	10 per cent.
Sugar	50 per cent.
Non-nitrogenous	10 per cent.
Salts	10 per cent.

Molasses contains from 1 per cent to 1.5 per cent of nitrogen, sometimes more. It is reported that sugar molasses possesses greater activity than sugar alone. Its nourishing value is high and it is easily assimilated. Being soluble it requires but little digestive action and in this way there is some saving of the vital energy of the organism. Molasses or sugar is readily diffusible, the osmotic processes are rapid and the passage through the intestinal tube into the circulation is not prolonged. Because the osmotic action is rapid, it is doubtful if there is complete oxidation of the sugar. Assuming that the blood is not able to supply sufficient oxygen for complete transformation, there probably results a stored up energy for subsequent tissue and fat formation.

Kellner found molasses to be four times as valuable for flesh production as ripe wheat straw. Meat from molasses-fed cattle has been pronounced of first class quality.

As compared with sugar, starch must undergo considerable modification and various changes before it can undergo assimilation.

Up to the present there has been no record of toxic effects from molasses feeding. Occasionally diarrhoea has been reported, presumably due to the salts in the molasses ; on the other hand some

have reported constipation, which has usually been corrected by the addition of a little bran to the feed.

Some untoward effects and inconveniences incident to the use of molasses have been reported. It has been believed by some that molasses tends to cause miscarriage in pregnant cows and that in young animals it appears to have a tendency to cause softening of the bones, unless calcium phosphate be added to the diet.

As examples of inconveniences may be mentioned the smearing of the manger and parts of the stall, the body of the animal, clothing, stable implements, and serving to attract the flies in warm seasons. In summer there is some danger of fermentation and the bursting of the barrel. As a result of fermentation there is a loss of sugar practically rendering the molasses unfit for use. With a good grade of molasses, the keeping qualities are good and there is not much danger of fermentation. It should contain not over 20 to 22 per cent of water. If there is 25 per cent of water there is danger of change.

Experiments.

Experiments in molasses feeding were conducted upon three horses at the New York State Veterinary College. No. 1 was under observation from December 21, 1903, to April 2, 1904. No. 2, from January 18 to February 4, 1904. No. 3, from February 5 to April 18, 1904. These animals were brought to the college to be disposed of. They were all well along in years and were not therefore in the best of condition.

They were under observation for a week before the experiments began in order to determine as well as possible their normal conditions. After the experiments were concluded, the observations were still continued, upon two of them for a week or more longer. A total of eighty examinations of the urine were made and the body weight was taken at regular intervals throughout the whole period of observation.

No 1 was a mare badly affected with the heaves, but otherwise was apparently in very good condition. Her age was estimated at 12 years. Her weight, the evening the experiment was begun, was

892 pounds. She was kept in her stall throughout the experiment and received no exercise further than a walk to the scales three times a week, a distance of about one-eighth of a mile.

Beginning December 21, her urine was examined daily up to December 25. The average of these determinations is shown in the following table :

Specific Gravity	1.041
Solids	95.53 per 1000
Chlorides	13.449 "
Sulphates	2.25 "
Phosphates	0.8375 "
Urea	35.25 "
Albumen	absent
Sugar	absent

The formula recommended by Dr. Berns was used in a modified form, corn meal being omitted and some oats substituted. Because the mare was doing no work she was put on half rations. For the month previous to the experiments she had been getting about 1.5 pints of oats ; 2.5 quarts bran and 6 lbs. of wet hay twice daily.

On the evening of December 24, she was put on the following ration :

Molasses	1 pint
Water	3 pints
Cut hay	2.5 lbs.
Oats	1 lb.
Coarse bran	2 qts.

The hay, oats, and bran were mixed and the diluted molasses slowly added and mixed thoroughly. This was refused at first, but the feed was all gone the next morning. After three or four days she ate the mixture readily. She was fed morning and night.

On December 28, her weight was 878 lbs., showing a loss of 14 lbs. since the 24th. As she ate her bedding and seemed hungry, it was thought best in connection with her loss of weight, to increase the ration to the following amount :

Molasses	1 qt.
Water	3 qts.

Cut hay	5 lbs.
Oats	1 pt.
Bran	2 qts.

The average of two urinary examinations taken since the 24th, and the period of increased ration gave the following results :

Specific gravity	1.031	
Solids	73.395	per 1000
Chlorides	8.089	"
Sulphates	1.5	"
Phosphates	1.08	"
Urea	20.	"
Albumen		absent
Sugar		absent

Comparing the two tables there is found to be a loss in all of the solids except the phosphates, which are increased.

In spite of the increased ration the weight of the animal continued to decrease and she did not regain her weight of December 28 until January 12. She had been weighed seven times in the interval and the average of these weights was found to be 865.39 lbs. Seven urinary determinations were also made during this period. The average of these is as follows :

Specific gravity	1.0424	
Solids	98.85	per 1000
Chlorides	15.80	"
Sulphates	1.85	"
Phosphates	2.	"
Urea	13.14	"
Albumen		absent
Sugar		present

On December 30 a trace of sugar was noticed in the urine. This increased somewhat in amount later and averaged about 0.33 per cent to 0.42 per cent. A comparison with the other urinary table shows that during this period of decreased weight there was an increased amount of solid constituents in the urine, except urea, which had fallen to nearly one-third of the amount found in the

normal urine. The sulphates are also somewhat lower than found in the normal but higher than in table No. 2.

During the next period from January 12 to January 25 the animal was weighed 7 times and the average of these weights amounted to 872.9 lbs., a gain over the preceding period but still about 20 lbs. less than the normal weight. Six urinary examinations were made during this period with the following average :

Specific gravity	1.0391	
Solids	91.258	per 1000
Chlorides	11.571	"
Sulphates	2.08	"
Phosphates	1.98	"
Urea	13.08	"
Albumen		present
Sugar		present

With a slight increase in weight there is a corresponding decrease in the urinary solids except in the case of the sulphates. On Jan. 18 the presence of albumin was noted. It was also present on Jan. 20 and Jan. 22 but had disappeared by Jan. 25.

On Jan. 25 there was added to the ration 4 oz. of dried blood from which the serum had been previously removed. The addition of the blood did not lessen the animal's eagerness for food. No further change was made in the diet until Feb. 8. During this period the animal was weighed five times and the average weight was 883.6 lbs., a gain of 10.5 lbs. over the preceding period. Five urinary examinations were also made with the following average :

Specific gravity	1.0402	
Solids	93.666	per 1000
Chlorides	———	
Sulphates	0.8	"
Phosphates	1.27	"
Urea	14.2	"
Albumen		absent
Sugar		present

Owing to an error the chlorides were not correctly reported and they are therefore ommitted. In spite of the increased albumen in

the diet there was no appearance of it in the urine although the sugar persisted.

On Feb. 8 the diet was again changed by reducing the amount of molasses to 1 pt. for each ration until Feb. 15. The horse was weighed four times during this period and the average weight obtained was 885.7 lbs. showing a gradual gain. Four urinary examinations were also made with the following average :

Specific gravity	1.043	
Solids	105.19	per 1000
Chlorides	———	
Suphates	trace	
Phosphates	1.13	"
Urea	23.	"
Albumen	absent	
Sugar	present	

The gain in urea is noticable. In the urine of Feb. 15 it was found that the sugar had disappeared, probably on account of the lessened amount of molasses in the ration.

From Feb. 15 to Feb. 22 no molasses was fed. The ration consisted of :

Bran	3 qts.
Oats	1 pt.
Long hay	6 lbs.

This was fed morning and night. The horse was weighed three times in this period and gave the average weight of 889.1 lbs. Three urinary examinations were made with the following average :

Specific gravity	1.038	
Solids	85.54	per 1000
Chlorides	4.967	"
Sulphates	trace	
Phosphates	0.60	"
Urea	32.9	"
Albumen	absent	
Sugar	trace	

The gain in urea and decrease in phosphates is very noticable. Although the animal received no molasses a trace of sugar appeared during the middle of this period and persisted.

On Feb. 22 she was given a pint of molasses diluted with water, sprinkled over her hay. On Feb. 25 her weight was 896 lbs., a gain of 6.9 lbs. over the previous period or a gain of 4 lbs. over her original weight at the beginning of the experiment Dec. 24. Urinary examinations were made Feb. 25 and Feb. 27 with the following average :

Specific gravity	1.040	
Solids	93.20	per 1000
Chlorides	4.362	"
Sulphates	trace	"
Phosphates	0.75	"
Albumen		absent
Sugar		present

On Feb. 27 the experiment was discontinued, but the animal was kept under observation until April 2. During this period she was weighed 12 times and an average weight of 861.8 lbs. obtained. Eleven urinary examinations were made and these averaged as follows :

Specific gravity	1.0426	
Solids	99.34	per 1000
Chlorides	3 998	"
Sulphates	trace	
Phosphates	1.25	"
Urea	32.9	"

Traces of sugar appeared Mar. 1 and Mar. 5. Traces of albumen also appeared Mar. 12 and Mar. 17. No positive tests for these substances were obtained at any other time during this period.

The condition of the animal through the molasses period was excellent ; her coat presented a fine appearance and her general health was good. There was no evidence of either constipation or diarrhoea, and no noticeable effect seemed to be produced upon the heaves. At times she was quite frisky and playful. When she was put on her former ration without molasses, a marked falling off took place as shown by the average loss of 34.2 lbs. in weight and lessened vigor generally. A summary of the urinary examinations is shown in the appended table :

Horse No. 1.

Date	Weight	Sp. Gr.	Solids	Chlor.	Sulph.	Phosph.	Urea	Alb.	Sugar
Dec. 21-25.	892	1.041	95.53	13.45	2.25	0.84	35.25	------	------
Dec. 25-28.	878	1.031	73.39	8.09	1.5	1.08	20.	------	------
Dec. 28-Jan. 12.	865	1.042	98.85	15.80	1.85	2.	13.14	------	present
Jan. 12-25.	873	1.039	91.29	11.57	2.08	1.98	13.08	present	"
Jan. 25-Feb. 8.	883.6	1.040	93.66	----	0.8	1.27	14.2	------	"
Feb. 8-15.	885.7	1.043	105.2	----	trace	1.13	23.	------	"
Feb. 15-22.	889.1	1.038	85.54	4.97	"	0.60	39.3	------	trace
Feb. 22-27.	896	1.040	93.20	4.362	"	0.75	35.5	------	present
Feb. 27-Apr. 2.	861.8	1.0426	99.34	3.998	"	1.25	32.9	------	------

The urinary figures in this table represents parts per 1000.

No. 2 was a mare well along in years and in good condition. Her weight, averaged from four weighings before the experiment, was 912 lbs. Her ration had been four quarts of bran and 5 or 6 lbs. of long hay morning and night. Daily tests were made of her urine from Jan. 18 to Jan. 25 inclusive, and the normal average was as follows :

Specific gravity	1.0342	
Solids	79.88	per 1000
Chlorides	7.722	"
Sulphates	1.	"
Phosphates	1.63	"
Urea	34.2	"
Albumen		absent
Sugar		"

On the evening of Jan. 25 the molasses ration was begun (morning and night) as follows :

Molasses	1 qt.
Water	3 qts.
Bran	3 qts.
Cut hay	5 lbs.

Like No. 1 she refused her feed at first, but had cleaned her box by the next morning. The next day there was a suspicious

trace of sugar in the urine which became more pronounced the day following and persisted until the end of the experiment, Feb. 4.

The average weight of the animal from Jan. 26 to Feb. 4 was 947 lbs., a gain of 35 lbs. over her normal weight. At no time during the molasses feeding did her weight fall to normal. During this period 7 urine examinations were made and the following averages obtained.

Specific gravity	1.0334	
Solids	77.88	per 1000
Chlorides	———	
Sulphates	0.7	"
Phosphates	1.47	"
Urea	13.5	"
Albumen		absent
Sugar		present

The great decrease in urea during the molasses ration is very striking.

On her way back from the scales, February 4, the mare fell on the ice and required assistance to rise. When returned to her stall she showed labored breathing and again lay down. She could not be induced to rise and as she seemed to be in a serious condition, she was killed and a post mortem held the next morning. The point of the ilium was found to be fractured; there was also some hemorrhage in the sub-lumbar region. Some frothy blood was noted near the duodenum. The diaphragm was ruptured and the intestines protruded into the thoracic cavity. Whether this resulted from the fall or not we do not care to say. Ruptured diaphragms are encountered occasionally in the dissection room, probably as a result of bloating. In this case there was an interval of about fifteen hours between the death and the post-mortem, and the cool February weather was not especially conducive to fermentation processes. In the dissection it was noticed that the tissues seemed to have a greasy "feel" suggesting the presence of fluid fat.

A series of five blood examinations was made before the molasses was fed and a similar number made while it was being fed. The average of each series is as follows:

	Red cells	Leucocytes
Before molasses	7,125,480	5,265
During molasses	5,768,228	5,434

The balance of the red cells is in favor of the normal period while for the leucocytes a small balance is shown in favor of the molasses. The result is interesting but more experiments are necessary before arriving at definite conclusions as to the effect of the molasses upon the blood.

No. 3. This subject was a mare well along in years, afflicted with sweeny but otherwise in quite fair condition.

From February 5 to February 13 her ration consisted of three quarts of oats and five lbs. of hay morning and night. Her average weight during this period was 704.5 lbs. Through an unfortunate misunderstanding the records of the normal urine were not kept completely and cannot therefore be used for reference, except that it was determined that no albumin or sugar were present.

A prepared food was used in this experiment, consisting of blood, molasses and chopped cereal. The proportions of the ingredients not being given.

The use of this food was begun on the evening of February 13 by withdrawing some of the oats and substituting the same amount of the new food, until on the 17th she was getting the proportion recommended by the manufacturers, namely: 1.5 quarts of oats 2.5 quarts of the prepared food with hay as usual. This proportion was continued until February 25. During this period her average weight increased to 727.1 lbs. Three urinary examinations were also made during this period with the following average:

Specific gravity	1.0366	
Solids	85.43	per 1000
Chlorides	———	
Sulphates	———	
Phosphates	2.19	"
Urea	16.6	"
Albumen		absent
Sugar	present Feb. 25	

On the evening of February 25 she was fed 5 quarts of the prepared food and the oats were altogether withdrawn. Hay as usual. This was continued until March 12. During this period her average weight increased to 765.4 lbs. Seven urinary examinations were made and gave the following average:

Specific gravity	1.0442
Solids	103.18 per 1000
Chlorides	4.664 "
Sulphates	trace
Phosphates	2.45 "
Urea	25.1 "
Albumen	present Mar. 10 and 12
Sugar	present

The gain in solids, especially urea, is noticeable. From the evening of March 12 to March 29 the ration was changed to 2 quarts of the prepared food with three quarts of bran. Hay as usual. The average weight for this period increased to 792.8 lbs. Six urinary examinations for this period averaged:

Specific gravity	1.0401
Solids	93.58 per 1000
Chlorides	8.36 "
Sulphates	trace
Phosphates	1.51 "
Urea	20.3 "
Albumen	at intervals
Sugar	at intervals decreasing

There was a little sugar present at the beginning of this period but it quickly disappeared. Albumen was found March 17, 24 and 26.

During the next period from March 29 to April 15 it was decided to give an increased amount of the molasses constituent; the amount of bran was reduced a little with a corresponding increase in the prepared food; to this was added 1 pint of molasses morning and night. The animal was weighed twice during this period and the average was 788 lbs. Four examinations of urine were made and gave the following average:

Specific gravity	1.0477	
Solids	111.26	per 1000
Chlorides	4.544	"
Sulphates	trace	
Phosphates	2.78	"
Urea	14.25	"
Albumen	present, not constant	
Sugar	present, not constant	

From the evening of April 15 to April 18 inclusive, the mare was fed 5 quarts of prepared food and 2 quarts of molasses twice daily, with hay in usual amount but of a poorer quality. On the 18 when she was killed her weight was 851 lbs., showing a gain of 146.5 lbs. over her normal average weight. The urine was examined April 16 and showed the following results :

Specific gravity	1.043	
Solids	111.19	per 1000
Chlorides	9.451	"
Sulphates	trace	
Phosphates	1.4	"
Urea	9.	"
Albumen	absent	
Sugar	pronounced	

The decrease in urea is pronounced and this may be correlated with the increased carbo-hydrate diet.

The following table is a summary of the urinary examinations.

Horse No. 3.

Date	Weight	Sp. Gr.	Solids	Chlor.	Sulph.	Phosph.	Urea	Alb.	Sugar
(Feb. 5-13 Normal)	704.5								
Feb. 13-25	727.1	1.036	85.43	----	----	2.19	16.6	------	Feb. 25
Feb. 25-Mar. 12.	765.4	1.048	103.18	4.664	trace	2.45	25.1	Mar. 10	present
Mar. 12-29	792.8	1.040	93.58	8.36	"	1.51	20.3	at intervals	at intervals
Mar. 29-Ap. 15.	788.	1.0477	111.26	4.544	"	2.78	14.25	present	present
Apr. 15-18	851.	1.043	101.19	9.451	"	1.40	9.	absent	present

In this table the urinary figures refer to parts per thousand.

Like No. 2 there was an increase in the body weight after the molasses food was used. The animal was in good spirits throughout and her coat was smooth and glossy. When the animal was dissected the same greasy condition was noted as in No. 2.

After the death of the animal sections of the liver and kidney were studied histologically. The following report was kindly furnished by Dr. S. H. Burnett of the Pathologic Department.

LIVER.—The liver shows marked parenchymatous degeneration throughout the entire lobules. The cells are swollen so that the capillaries are very narrow. The cells are coarsely granular and the nuclei pale. The central vein and the peripheral vessels are congested. There are a few leucocytes in the connective tissue surrounding the peripheral blood vessels. The conditions indicate acute parenchymatous hepatitis.

KIDNEY.—The glomeruli and vessels near them are congested; the epithelial cells of the convoluted tubules are swollen and coarsely granular; the cells of the straight collecting tubules have lost their granules and are clear, their nuclei seem shrunken.

In the medulla the epithelial cells of the smaller collecting tubules are swollen and coarsely granular while in the larger tubules the epithelial cells are clear; the nuclei seem to be shrunken.

The interstitial tissue in the medulla is thickened by a fibrinous exudate more markedly near the pelvis, while the tubules near the pelvis have mostly lost their epithelium. There is marked congestion especially in the middle portion of the medulla. The indications point toward acute mixed nephritis.

GENERAL CONCLUSIONS.

The various reports upon molasses feeding that we have encountered have been uniformly of a favorable nature, but seem to have been based upon external observations as to the general health and condition of the animals.

The fact that sugar appeared in the urine of all three of our experimental subjects, soon after the molasses was given, is interest-

ing and perhaps significant. The later appearance of albumen intermittently, in two of the cases, is also noteworthy. The presence of either of these substances is usually regarded as an abnormal condition and yet, during their appearance the general health of these animals seemed good, and they exhibited more vigor than before. Albumen and sugar serve as foods for the tissues, their undue loss through the kidneys would mean a drain upon the system, a distinctly pathologic condition. Their elimination intermittently or in small amounts may represent a physiologic condition, merely the removel of an excess of the given substance in the system.

With regard to the constituents of the urine, the most striking effect of molasses feeding was upon the urea. This constituent invariably fell considerably below normal when molasses was used. Perhaps, in a general way, this may be due to the fact that the molasses contained less material from which urea might be formed. In a carbohydrate diet the nutritive ratio is wide. (Beet molasses, however, has a ratio of 1 :6.5). When an increased body weight occurs, this may be due to the conversion of the albuminoid material in the ration into tissue forming substances and thus account for the diminished urea. In subject No. 1, however, there was at first diminished urea and decreased weight. As this subject was afflicted with a pathologic condition (heaves), it is not unlikely that the body metabolism was influenced and some irregular results produced in connection with the molasses feed. The pathologic conditions noted in No. 3 would likewise have an important influence upon the elimination of urea ; the diseased epithelial cells being no longer able to do their work properly, it might be expected that the urea would be stored up in the system.

The phosphates fluctuated considerably ; the sulphates, although fluctuating somewhat, had a marked tendency to diminish as the experiment progressed. The chlorides were unreliable on account of some errors in the early part of the experiments ; the later data showed that they had a tendency to diminish.

All of our experiments agree in the fact that abnormal constituents (sugar and some albumen) were found in the urine, soon af-

ter the molasses ration was begun. In the only case examined histologically, marked pathological conditions were present in the liver and kidney. It would be difficult, without further observations, to prove that these conditions were caused directly by the molasses; but the fact that all of the urines contained abnormal products seems to be significant in this connection.

We do not go so far as to state that the results above mentioned are present or are to be expected in all cases, where molasses is used as food. The title of our paper limits it distinctly to horses at rest and even here the results may not be uniform. Age is quite likely to be a factor. All of our subjects were quite well advanced in years and the tissues, more or less worn out with the wear and tear of advancing age, were doubtless either more susceptible or less responsive to any unusual demands made upon them.

In horses doing work it is quite reasonable to suppose that the effects we have described may not appear to any noticeable effect if at all. In general, a rich carbohydrate diet is productive of much energy. If this energy is used up in the accomplishment of work it is an economic arrangement so far as the body tissues are concerned. If on the other hand this energy is stored up in the system without adequate outlet the effect upon the tissues must be pronounced and the results that we have encountered might be expected.

Molasses is a concentrated food and an undue proportion in the system, under any condition, may be productive of more harm than good. Its value as a food is generally accepted, but, it seems to us there should be certain reservations as to the amount and time of feeding, dependent upon the age and amount of work done by the animal.

A careful study of the nutritive ratio in all rations into which molasses enters as a constituent is important.

THE SOURCE OF MUCIN IN THE URINE OF THE HORSE.

H. J. MILKS.

In a study of the urine of the horse, one of the most noticeable characteristics is the consistency. It is the rule, rather than the exception, to find it stringy and viscid. Indeed, it is only occasionally clear and of a watery consistency. It was due to this viscidness and the fact that there is some controversy concerning the origin of the mucin that I investigated the source of its secretion.

The work has been carried on with two views in mind : First, to clear up, if possible, the origin of the mucin ; and secondly, to work out its characteristics and to find a reliable test for mucin. Naturally, it has fallen under two heads : histological and physiological. The histological will be taken up first.

Several authorities were studied with a view of ascertaining the structure of the intra-and extra-renal passages. A summary of these will show that there is quite a diversity of opinion in regard to their structure, the general opinion, however, seems to be that there are no glands present, or, if present, are in very small numbers.

Piersol—Text Book of Histology.—The greater part of the renal sinus is occupied by the dilated ureter, the mucosa of which is covered with the stratified squamous epithelium, which comprises few layers of cells. The epithelium is termed transitional because of the rapid change from columnar, in the deep layer to squamous in the superficial strata. The tunica propriaor stroma of the mucosa contains a few racemose glands.

Böhm–Davidoff—Huber.—The renal pelvis, ureter, and urinary bladder are lined with the stratified transitional epithelium. A few mucous glands are met with in the upper portion of the ureter and pelvis. None are found in the bladder.

Stohr, Schafer, and Stricker do not mention the presence of glands, while Szymonowicz and MacCullum say that glands are wanting in the pelvis and ureter mucosa.

It must be remembered that the above authorities refer particularly to human histology. In none did I find a description of the urinary apparatus of the horse. The following books refer more to the latter.

Malkmus—Clinical Diagnostics.—The mucin in the urine comes from the bladder.

Chauveau—Anatomy of the Domestic Auimals.—Although, this work treats of the microscopical as well as the gross anotomy, nothing is said concerning the presence of glands in the urinary passages.

Ellenberger und Günther—Histologie der Haussaugetiere—The pelvis of the kidney is lined with the transitional epithelium. The mucosa, in the horse, is partly gland containing. Also in the dog, glands are sometimes found.

It will be observed from the preceeding, that the structure of the intra-and extra-renal passages is not well agreed upon. Some experiments upon a living horse, a few years ago, by Drs. Fish and Fisher, in which, by ligating the ureters, they demonstrated that the bladder was not the sole source of supply. They found that the urine between the ligature and kidney was of a much more viscid nature than that in the bladder; they even compared it to egg albumen in its consistency.

The material used in the histological work was taken from horses recently killed. In one instance a kidney was removed from a horse under anaesthesia.

Technic.

The kidneys were studied, both as to their gross and microscopical anotomy. For the former, both the fresh and hardened specimens were examined. For the latter, they were fixed by both the mercuric chloride and formalin methods. Only paraffin was used for embedding purposes. On account of the large size of the kidney, serial sections were not used. Blocks were cut from various sections of the gland, labeled, and a drawing made showing their exact location. Various stains were used: hematoxylin and eosin,

hematoxylin and orange G, eosin, methylene blue and eosin (Manns) and muchaematin.

Gross Anatomy.

By making a cross section of the kidney, the cortex, medulla, and pelvis will be readily distinguished, as outlined in Fig. 1. In this drawing it was not the purpose to show the different parts in detail simply to indicate them. An examination of the pelvis shows it to be rather extensive, and its mucosa roughened and thrown into folds.

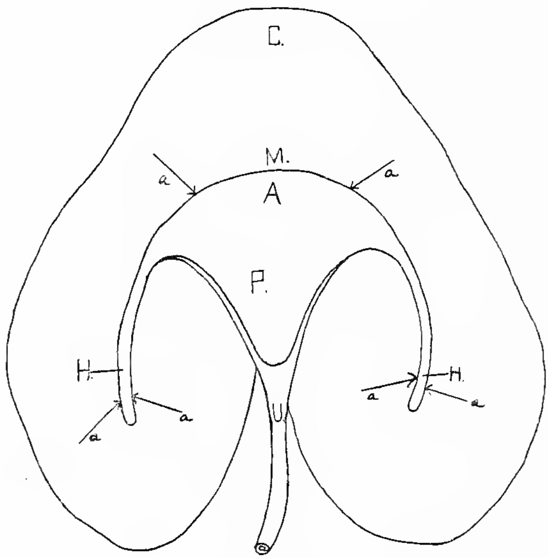


Fig. I.
Cross section of kidney of a horse.
C. Cortex. M. Medulla. P. Pelvis.
H. H. Horns of pelvis. U. Ureter.

Upon closer examination, leading in either direction from the main pelvis, are the horns of the pelvis H. H. Fig. 1. These are, as a rule smaller than is indicated upon the diagram. Their mucosa is smooth. If the examination is made with a hand lens, it will be seen that the pelvis contains the openings of the uriniferous tubules. This is also true of the horns of the pelvis. These tubules open into the pelvis in different directions, as is indicated by the arrows, a. a. Fig. 1.

Sections were made from different areas of the pelvis, horns of the pelvis, and other portions of the gland, *i.e.*, cortex and medulla. Sections taken from the main pelvis (region A, Fig. 1), and stained with hematoxylin thirty minutes, and eosin ten seconds, showed the lining epithelium of the transitional variety, consisting of few layers of cells. Beneath this and imbedded in a connective tissue stroma were numerous glandular structures, composed of simple columnar epithelium, the cells being rather long, well defined, and having their nuclei, oblong in shape, lying near their bases. Within the cells of the glands were numerous granules, more abundant in that part of the cell nearest the lumen of the gland. They had, in some cases, evidently passed without the cell.

The glands were found to belong to the compound tubular variety, and, as before stated, were made up of the simple columnar epithelium, Fig. II is a drawing made from one of these glands.

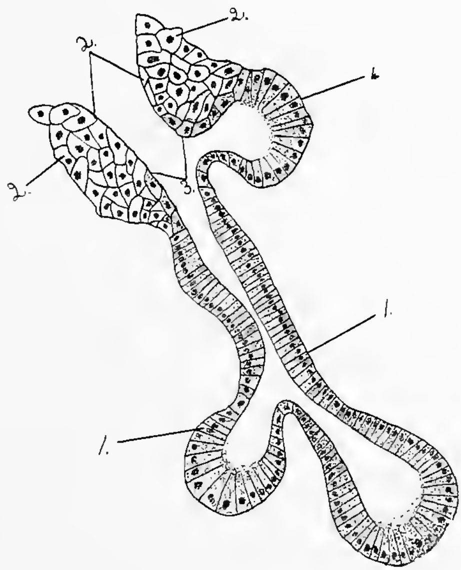


Fig. II.

Isolated gland from pelvis of kidney of horse.
(Drawing made with Camera Lucida.)
1 and 3 are secreting cells from pelvis.
2 Transitional epithelium of urinary passage.

Besides the general glandular outline, it will be seen that the change from the columnar cells of the gland to the transitional lining the pelvis is gradual. As the columnar cells 1. approach the surface they become shortened and are underlaid by a layer or two of the transitional variety; 2, 2, represents the transitional epithelium underlying the shorter but thicker secreting cells 3, 3. Cells represented by 1 and 3 are secreting cells; those by 2 are non secreting.

The glands were further studied with regard to their reaction to certain stains. Mann's methylene blue and eosin was first used. This is supposed to stain mucous secretions and connective tissue a deep blue.

In the section from the kidney it stained only the connective tissue; the secretion from the cells did not stain at all. However, it revealed, very nicely, the fibers of connective tissue in which the glands were embedded.

A stain described as muchaematin by Robert R. Bensley of Chicago in his publication "The structure of the Glands of Brunner" was then used. It is prepared and used as follows:

Aluminium Chloride	0.5 gm.
Pure Haematin	1.0 gm.
70 per cent Alcohol	100. cc.

Triturate the aluminium chloride and haematin in a mortar, gradually adding the alcohol, and filter. The solution is then allowed to stand for a week, during which time it deepens in color and its mucin staining power is increased.

Slides are treated with benzol, then absolute alcohol, flooded with the stain, and watched under the microscope until the cell contents became deeply stained; wash quickly with 95 per cent alcohol, dehydrate, clear, and mount in balsam.

The preparation has no effect upon the protoplasm of the cells. While it stains a deep blue the secretions from the following sources; mucous cells from the sub-maxillary, sublingual, palatine, tracheal, oesophageal glands, gastric epithelial cells, cells of the cardiac end of the stomach, cells of the pyloric glands, the chief

neck cells of the fundus glands of the stomach, goblet cells and cells of Brunner ; except the dark tubules of the rabbits glands.

It does not stain the demilune cells of the salivary glands, cells of the parotid, serous cells of the submaxillary or sublingual, serous portions of the palatine or tracheal glands, nor the ferment forming cells of the pancreas and fundus glands of the stomach.

Fig. III.
Pelvis of kidney of horse.x88.
Section stained with Muchaematin. The black areas represent the stained mucin.

Sections removed from region A (Fig. 1) were stained with muchaematin, and gave the following reaction : the protoplasm did not react at all ; the secretion, however, was stained a deep blue. This was found in more abundance near the lumen of the gland and was of a granular appearance. Under the 1/8 objective, the secretion stands out as a feathery mass (see Fig. III). In this figure an idea of the intensity of the stain and its selective action, will be obtained. A section to which mucous was adherent was stained in a similar manner and it was found that the staining properties of the secretion within the cell were identical with those of the secretion without the cell.

To substantiate the proof that the substance in the cells was mucin, the experiment was made of dissolving it out by means of an alkaline fluid. As potassium carbonate is the salt to which the alkalinity of the urine of the horse is due, it was used as the solvent, employing the following method: A number of sections were fastened to slides, carried through benzine, alcohol, and water, then placed in a jar containing a 5% solution of potassium carbonate, and put in an incubator at 37° C. At intervals sections were removed, washed in water, and then in a 0.1% solution of acetic acid, again washed in water, transferred to alcohol, stained with muchaematin, cleared and mounted in balsam. In sections subjected to the solvent action of the fluid for (12) to eighteen (18) hours the mucin had almost entirely disappeared.

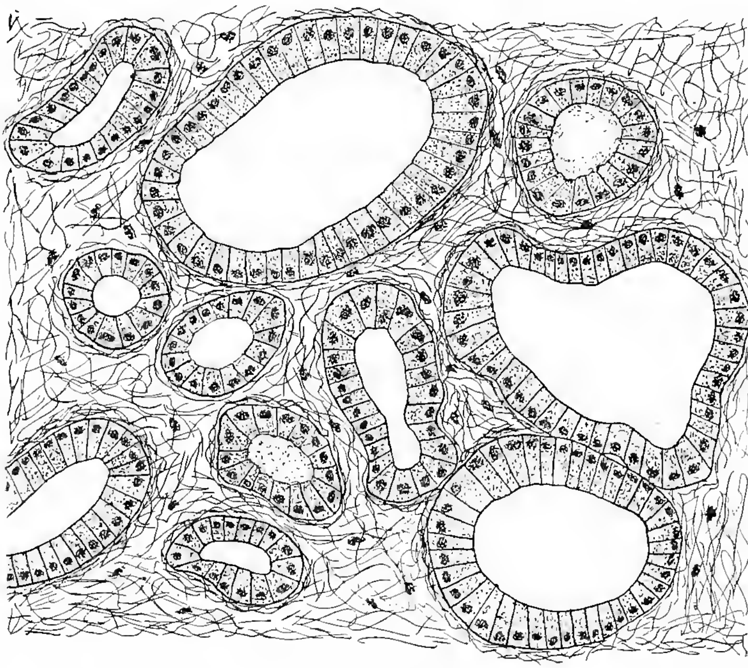


Fig. IV.
Section of ureter of horse showing glands.
Drawing made by Camera Lucida.

Further examination proved that mucous follicles were constantly present in the main pelvis (P, Fig. I.) but that in the horns of the pelvis (H H Fig. I.), they were not found. Neither was I able to obtain any reaction to the muchaematin from any other area of the kidney except the main pelvis.

Ureters.

Glands identical with those of the pelvis were found in large numbers in the upper portions of the ureters, extending, probably, not more than five (5) or six (6) inches from the kidney toward the bladder. These glands gave the same reaction to the muchaematin as did those of the pelvis. Fig. IV, is a drawing made from a section of one of these glands.

Bladder.

No mucous follicles were found in the bladder, although many sections from different areas were studied.

Physiology.

Although much work has been done upon the subject of mucin in the urine of human beings, very little study has been made of its presence in the urine of the horse, and yet, in the latter secretion, it undoubtedly exists in much greater proportions.

Normal horse urine is viscid and stringy and may be drawn into threads. It is rarely of a watery consistency. That its viscidness is not due to contamination from the genital passages is proven not only by the fact that urine drawn directly from the bladder has the same syrupy appearance, but also by the experiments of Drs. Fish and Fisher, in which they ligated a ureter of a horse under anaesthesia, and although no qualitative tests were made, concluded it to be thicker than that in the bladder, even comparing it to egg albumen in consistency. This experiment has been repeated by me, and the urine analyzed so far as the amount would permit. In each case a sample was taken from the bladder

and used as a control. I found the urine from the ligated ureter to be so thick that it was necessary to use considerable pressure to expel it from the ureters and pelvis of the kidney. In some cases it could not be expelled at all, and, upon opening the pelvis, was found so thick that it could be lifted out with the hands. The following analysis will give a fair idea of the composition of the two urines.

Horse No. 1. Male.	Ureter Ligated Two Hours.
Urine from bladder.	Urine from kidney above the ligated portion.
Consistency, slightly viscid.	Thick like egg albumen.
Specific Gravity. 1040.	1040
Albumen. None present.	A trace only.
3cc. urine + 4 cc. acetic. acid + centrifuge for 3 min. = Trace of ppt. Mucin.	1 cc. of precipitate Mucin.

No. 2. Male.	Ureter Ligated Two Hours.
Consistency. Slightly viscid.	Thick, Syrupy.
Specific Gravity. 1040.	1045.
Albumen. Not present.	Trace only.
3 cc. urine + 4cc. alcohol + centrifuge for three min. = $\frac{1}{5}$ cc. of precipitate. Mucin.	$\frac{3}{8}$ cc. Precipitate. Mucin.

No other tests were employed on account of the small amounts of urine obtained from the ligatured ureter.

According to a classification by Hammersten but attributed to Hoppe-Seyler and Drechsel, mucins are proteid bodies, classified as compound proteids, under the subhead of glycoproteids.

Mucins are colloid substances whose solutions are thready and which, when treated with acetic acid, give a precipitate, insoluble in an excess of the acid, and, upon boiling with dilute mineral acids, yields a substance capable of reducing copper oxyhydrate.

All mucins contain carbon, nitrogen, hydrogen, sulphur, and oxygen. Compared with albuminous bodies they contain less nitrogen and, as a rule, less carbon. As immediate decomposition

products, they yield an albuminous substance on the one hand and a carbohydrate, or allied body, upon the other. All give a reducible substance, if boiled with dilute mineral acids.

True mucins are secreted by the larger mucous glands. By the action of superheated steam, mucin gives off a carbo-hydrate. This is not always true, as the submaxillary mucin gives off a substance containing nitrogen. On boiling with dilute mineral acids, acid albumen (syntonin) and bodies similar to albumoses and peptones are given off. Also a carbo-hydrate that has not been closely studied. With stronger acids, they produce among other substances, leucin, tyrosin, levulic acid, etc. Mucins are not coagulated by heat, are slightly soluble in neutral or alkaline solutions and are soluble in lime water.

The methods commonly employed to isolate mucin are to precipitate them by adding alcohol, in various proportions, from equal parts of each to five parts of alcohol to one of the solution, filter, wash the precipitate well with alcohol and then allow to dry. Or it may be purified by redissolving in lime water and again precipitating with acetic acid.

The above methods have been used many times. Both the filtered and unfiltered urines were studied. Upon the addition of the alcohol, a copious, white, flocculent precipitate appeared. When the precipitate is purified, as is explained above, it becomes lighter in color and more flaky. The separation was continued until a quantity of the material was obtained. Portions of this were treated with dilute sulphuric acid. It was not readily soluble but dissolved upon boiling, giving a clear, yellowish brown liquid, resembling, in color, the urine of the horse. Solutions were boiled for twenty minutes and at the end of that time tested for syntonin and reducing substances.

For syntonin, the method followed was to add a little litmus to the solution and an excess of a dilute solution of potassium hydrate. The contact method was employed and a precipitate at the line of the two fluids indicated acid albumen. It was not possible to obtain positive results in each case, but in many cases they were

obtained. For reducing sugars, Trommers test and Fehlings solution were used.

The precipitate from the alcohol was but slightly soluble in water and but little in alkaline solutions. Indeed, not enough of it could be dissolved to obtain any appreciable amount in a fluid. Neither would solutions of it give positive reactions to any of the so called mucin tests.

The test most commonly used to detect mucin in human urine is to dilute with an equal amount of water, and then add acetic or citric acid. The contact method is the one most commonly used, and acid being introduced first. If mucin is present, a more or less pronounced precipitate appears at the line of contact. Acetic acid saturated with salt has been advocated by some, using the same method as the above. Some, also, advise making more alkaline before testing.

Horse urine treated as above does not give very satisfactory results. Acetic acid has been used in various proportions, thus: glacial, commercial, commercial saturated with salt. Citric was used in twenty per cent, ten per cent, five per cent, and a two and one half per cent solutions. The more favorable results were obtained with the stronger acids. No precipitate was obtained with the weaker acids. As a rule, if the solution was made more alkaline with ammonium hydroxide, the tests were more satisfactory and the precipitate more distinct.

Conclusions.

The mucin in the urine of the horse comes, in the main, from the mucous glands situated in the pelvis of the kidney. A very small amount comes from the glands in the upper part of the ureter; none of it comes from the bladder. That while suitable means have not yet been devised for isolating and detecting mucin in horse urine, yet, without doubt, the substance is mucin, as is proven by the tests described above. That of the tests described, the one in which the urine is made more alkaline before testing is the most satisfactory.

Bibliography.

But few articles were found bearing upon the subject of mucin in the urine of the horse. The following text-books have been drawn from quite freely :

Meade Smith.—Physiology of the Domestic Animals.

Capt. Fred Smith.—A Text-book of Veterinary Physiology.

James Law.—Veterinary Medicine. Vol. III.

Hammarsten.—Physiological Chemistry.

Allen.—Commercial Analysis.

Salkowski.—Chemical Physiology.

Heitzman.—Urine Analysis and Diagnostics.

Tyson.—Practical Examination of Urine.

Bensley, R. R.—Structure of the Glands of Brunner. (Bulletin, University of Chicago.)

THE EFFECT OF CERTAIN DRUGS UPON METABOLISM AS DETERMINED BY URINARY EXAMINATION.

J. A. MADDEN.

The drugs investigated were: salicylic, benzoic, sulphurous, and boric acids, also borax and echinacea. The doses in all cases were minimum and the results obtained may, on this account, vary somewhat from those of other investigators. The methods adopted in the urinary examinations were those commonly used in clinical work and are believed to be sufficiently accurate for comparison of the normal and drug periods. The centrifuge was used for the determination of the chlorides, phosphates and sulphates. The tests were, at first, checked by the volumetric determinations commonly in use and the value of each 0.1 cc. of ppt. in the centrifuge determined on the basis of parts per 1000. As a great many examinations were to be made, it was believed that the centrifuge method would be the most expeditious and accurate enough for ordinary purposes. For the urea determinations, the Doremus Ureometer, as modified by Hinds, was used with the sodium hypobromite solution. The apparatus was tested with a solution of urea of known percentage and was found to be accurate within a slight fraction of a gram. No uric acid determinations were made and in none of the tests were albumen or sugar found to be present.

The general plan of the investigation was, in each case, to collect the total amount of urine for twenty-four hours and take from this a sample for analysis. Seven days (one week) was the limit of each period. Before the drug was taken, seven analyses of the urine were made. This may be referred to as the normal period.

Following this, the drug was taken for one week and this will be designated as the drug period. The average of each seven examinations is taken as representative of the condition of the urine

for that period—say the normal ; and this average is compared with that obtained from the drug period, the amount of the constituents in all cases being determined in grams or cubic centimeters for the twenty-four hours.

Except in the case of sulphurous acid, five grains of each drug were taken three times a day before meals for one week with a normal period between the use of each drug.

Salicylic Acid. According to Rideal, (1) this drug is not a harmless remedy and may produce a disintegrating effect upon the blood corpuscles.

The salts of salicylic acid may cause albuminuria, indicating an irritating effect upon the kidney, perhaps on account of the formation of phenol (2).

H. Leffman, (3) after a number of experiments, concluded that salicylic acid in all forms, natural, crude or refined, is distinctly antagonistic to most enzymes, especially those that convert starch. He showed that in the proportion of 1 to 20000 it retarded the con-conversion of starch in the ratio of 245 to 174, while 1 to 1000 entirely prevented conversion, both with diastase and pancreatic ferments.

Chittenden (4) found that salicylic acid and salicylate of soda greatly retard peptic digestion.

Rideal (1) thinks that if the drug is allowed to mix or penetrate the food, that chronic dyspepsia and other symptoms would appear by the relatively large amounts that would accumulate in the system. There seems to be evidence, that like lead and arsenic it has a cumulative action.

Bronacdel (5) especially characterizes salicylic acid as being injurious in cases of weak or diseased kidneys, by its cumulative action in the system.

Luthye investigated the action of the salicylates on the urinary tract, and found in every case, evidence of desquamative irritation in the kidneys, urinary passages and the bladder appeared inflamed. The urine contained tubular casts and its condition did not return to normal for two or three weeks.

Experiments (6) on calves by feeding them milk without salicylic acid and milk containing the drug in the proportion of 1 to 1000, there was found a difference of 3.48% protein and 4.56% fat, in favor of the untreated milk.

Antiseptic and Preservative Uses. The strength of salicylic acid required for killing bacteria has been variously given by different observers. Vallin claims "that its action on ferments and microbes is often only temporary; the ferments and bacteria rapidly become used to their new surroundings and the following generations that succeed, resist doses that have been fatal to their ancestors. For this reason alcoholic beverages which can only be preserved by the aid of salicylic acid require large amounts, as high as 1.5 grams per liter. Salicylic acid is considered a convenient antiseptic, but it gives no absolute guarantee, and its power is limited. This drug has been largely used for preserving perishable foods in the proportion of four to eight grains to the pint or pound. It is used to aid the preservation of fruit, beverages, milk, fish, meats and eggs.

Experimental. After six urinary examinations to determine the average for the normal urine, as previously explained, the writer took five grains of salicylic acid in capsules before meals for seven days. The urine was collected and examined as before and the average taken for the Salicylic period. An unpleasant and somewhat burning sensation in the stomach was noticed soon after taking the drug. The appetite and general system appeared to be somewhat depressed and there was a continuous but not severe pain in the region of the kidneys. The following table shows the effect upon the urine.

Normal Period	Amount	Sp. gr.	Solids	Chlorides	Sulphates	Phosphates	Urea
Dec. 29–Jan. 3, '04							
Average of							
6 Examinations	991	1027.6	63.169	7.563	1.927	2.084	28.22
Salicylic Period							
Jan. 4–10							
Average of							
7 Examinations	841	1028.5	53.903	7.200	2.292	1.957	27.494

Maximum of Normal Period	1220	1030.	69.900	9.333	2.500	2.415	32.00
Maximum of Salicylic Period	1150	1032.	69.570	15.884	4.025	3.220	36.80
Minimum of Normal Period	830	1024.	57.510	5.780	1.927	1.830	23.24
Minimum of Salicylic Period	485	1026.	36.132	3.378	1.350	1.358	17.46

A comparison of the two averages shows a decreased amount of urine, a higher specific gravity and a decrease in all of the constituents except in sulphates, during the drug period.

BORAX. Lubrech (7) experimented upon dogs, by giving them five grams of borax per day. After the sixteenth day, the dogs showed symptoms of violent intestinal inflammation with hemorrhage; appetite being diminished. There was howling and whining indicating severe pain. This showed that borax in two great concentration is liable to excite intestinal symptoms and irritation.

Henry Leffman (8) claims that borax in very large doses tends to retard the assimilation of proteid and fatty food, increasing notably the weight of feces and their contents of nitrogen and fat. Excessive doses cause diarrhoea. In moderate doses, borax showed little or no interfering action with either starch or proteid digestion.

Chittenden and Gies (9) experimented on dogs with borax and analyzed both urine and feces. They arrive at the following conclusions: 1. That the animal increased in weight, not from the laying on of fat, but to the diminished secretion of water. 2. The specific gravity of the urine was increased, rising from 1017–1018 to 1022–1027, dropping back as the experiments were discontinued. 3. The reaction of the urine, after the first day of borax, changed from an acid to an alkaline reaction. 4. The salt was rapidly eliminated, for thirty-six hours after close of borax period no trace of it could be found. 5. Has no cumulative action in the system. The amount daily per dog was five grams.

Experiments in feeding calves (6) on milk with and without

borax. The amount of borax given was 1 of borax to 675 of milk. The determinations showed there was 1.3 per cent protein and 0.2 per cent fat gain in amount in favor of the untreated milk. The borax appeared to prevent digestion to a slight extent.

Preservative Uses. Borax is used in the preservation of milk, cream, marjorine and butter principally. It is also used in the preservation of meats and fish.

Experimental. Five grains of borax were taken three times a day, before each meal, for a week. An occasional headache, some pain and uncomfortable feeling over the region of the kidneys were experienced. Micturition occurred during the night in this period. This had not been experienced before and did not occur later. The bowels appeared looser and a larger quantity of feces was passed. The appetite was in no way affected. The effect upon the urine is shown in the subjoined table :

Normal Period	Amount	Sp. gr.	Solids	Chlorides	Sulphates	Phosphates	Urea
Jan. 11–17 Average of 7 Examinations	989	1027.	62.10	6.84	1.89	1.81	29.30
Borax Period Jan. 18–24 Average of 7 Examinations	982	1025.7	58.42	6.39	1.26	1.74	26.61
Maximum of Normal Period	1200	1030.	72.60	7.65	2.25	2.13	33.70
Maximum of Borax Period	1325	1028.	74.06	9.01	2.00	2.30	33.00
Minimum of Normal Period	800	1024.	55.90	6.12	1.71	1.62	24.00
Minimum of Borax Period	700	1024.	45.64	4.76	0.70	1.35	19.60

A comparison of the averages shows there is a slight decrease in all of the constituents during the borax period.

Boric Acid. Dr. J. J. Evans, (10) in treating a case of cystitis with boric acid, and increasing the dose from ten to twenty grains three times a day, concluded that the drug had a toxic effect. After three weeks of treatment, an erythematous rash spread over the man's face, neck and head. This was followed by a sub-

cutaneous oedema and scaly dermatitis ; the salivary glands becoming enlarged, eventually the hair of the face and head fell off, inside a fortnight. In treating similar cases later, the same symptoms resulted.

Von Noorden, (11) shows that a 3.5 per cent solution of boric acid gave rise to a stomatitis, characterized by swelling of lips, gum, border of tongue, salivation, tenderness, and now and then superficial ulceration.

G. Merkel, (12) administered boric acid internally to thirteen patients for its assumed action, in doses of from one to two grams daily, in aqueous solution, for eight days. The polyuria that followed, even small doses, surpassed twice and even three times the normal amount, and boric acid could be detected for seventeen days after it had been discontinued. Seven of the patients complained of various gastric disturbances, colic and diarrhoea, while taking the drug, another of the patients who used insufflation of boric acid, was, after several days, affected with erythema.

Metabolism experiments (13) in which respiratory products were taken into account, indicated that boric acid increased the production of CO_2 and water vapor, and increased the clearage of fat, or carbohydrates in the body.

In experiments, (6) in feeding calves with milk containing preservatives, it was found that there was a difference of 2.52 per cent protein and 0.19 per cent. fat in favor of the untreated milk, against that containing boric acid. Boric acid appears to prevent digestion.

Chittenden and Gies (9) performed experiments on dogs with boric acid, from which the urine and feces were analyzed, and they drew the following conclusions :

1. Moderate doses up to five grams per day, even when continued for some time, does not influence proteid metabolism. 2. There was no specific influence on the general nutrition of the body. The body weight did not tend to increase. 3. Large doses 5–10 grams per day directly stimulates proteid metabolism, increases the excretion of nitrogen, also the sulphates and phosphates. 4. Excessive doses tend to cause an increase of mucus and diarrhoea.

Preservative Uses. Boric acid is used as a preservative for butter, cream, milk, hams and fish. Some writers think that meat preserved by boric acid is not diminished in nourishment and is more readily assimilated; others disagree and arrive at an opposite conclusion. Lehmann infers that it is not the boric acid that acts as the preservative, but rather the substances produced by it, *i.e.*, acid phosphates.

Experimental. Five grains of boric acid were taken three times a day just preceding each meal. The urine was collected and examined as in the preceding cases. Aside from some diuresis, no physical effects whatever were felt.

URINARY TABLE.

Normal Period	Amount	Sp. gr.	Solids	Chlorides	Sulphates	Phosphates	Urea
Jan. 25–31 Average of 7 Examinations	732	1028.3	45.650	11.960	1.056	1.360	20.57
Boric Acid Feb. 1–7 Average of 7 Examinations	859	1026.	51.262	16.396	1.246	1.388	20.97
Maximum of Normal Period	850	1030.	55.920	14.790	1.300	1.760	25.60
Maximum Boric Acid Period	1030	1030.	62.592	22.200	1.545	1.728	23.25
Minimum of Normal Period	625	1022.	41.400	9.900	0.425	0.9	15.60
Minimum Boric Acid Period	525	1022.	36.720	8.790	0.780	1.05	14.70

A comparison of the averages shows a lower specific gravity but an increased quantity of urine with higher constituents during the boric acid period. This indicates increased metabolism.

BENZOIC ACID. Julan de la Croix (14) in seventy-four experiments, with varying quantities, found that the least quantity that would prevent bacterial growth in fresh beef tea was 1 to 2800. To kill bacteria it required 1 to 410 and to sterilize spores 1 to 50.

Graham Brown (15) stated that sodium benzoate was superior to

quinine hydrochlorate and sodium salicylate in destroying the virus of diphtheria. He believed even that by saturating the human system with benzoic acid, by repeated hypodermic injections, the system was rendered almost insusceptible to inoculation with diphtheria.

Gosslin and Robin, (16) proved that in disorders of the bladder attended with ammoniacal urine, that benzoic acid taken internally rendered the urine acid, preventing the precipitation of insoluble phosphates and the formation of carbonate of ammonium and poisonous salts by the urinary bacteria. They used it in uremia successfully, in amounts of 1 to 4 grams daily, dissolved in glycerine and water.

Wernitz, (17) declares that pepsin is neutralized by 1 to 200 and others by 1 to 300 of benzoic acid or benzoate of soda.

In order to determine whether benzoic acid increased the acidity of the urine, Dr. William Ashhurst, (18) experimented upon dogs. The urine of the dogs was tested for a number of days previous, afterwards the dogs received hypodermically 1 gram and finally 2 grams daily. From the experiments he drew the following conclusions; 1. It had an inconstant diuretic effect, accompained by a slight diminution of the acidity of the urine. 2. Retardation or absolute prevention of the occurrence of alkaline fermentation. 3. It had a germicidal and inhibitory action on the growth of certain micro-organisms, either within the bladder or introduced from without into the urine after voiding.

Preservative Uses. A saturated solution in water delays the putrefactive changes taking place in animal matter. It is used in preventing fats from becoming rancid as in "adeps benzoinatus." Added to milk in small quantities, it prevents coagulation, but its action is not as lasting as the fluorides, probably owing to the benzoic acid being more easily decomposed by some of the organisms.

Experimental. Five grains of benzoic acid were taken three times a day in capsules before each meal. A general feeling of depression appeared to result from the use of this drug. There was a dull headache and dull but rather continuous pains over the region

of the kidneys. The appetite and tone of the stomach appeared to be lessened.

URINARY TABLE.

Normal Period	Amount	Sp. gr.	Solids	Chlorides	Sulphates	Phosphates	Urea
Feb. 22–28							
Average of							
7 Examinations	846.4	1026.85	52.27	15.25	1.37	1.51	26.54
Benzoic Acid Period							
Feb. 29–Mar, 6, '04							
Average of							
7 Examinations	824.2	1026.85	51.52	13.68	1.44	1.39	23.75
Maximum of							
Normal Period	1000.	1030.	64.65	18.46	2.30	1.85	30.00
Maximum Benzoic							
Acid Period	1070.	1030.	59.81	18.19	1.70	1.53	28.90
Minimum of							
Normal Period	700.	1022	45.37	12.44	0.90	1.35	17.50
Minimum Benzoic							
Acid Period	700.	1024	42.35	10.35	1.05	1.12	19.50

The average periods show a gain in sulphates for the benzoic acid period. For the other constituents there is a slightly higher amount for the normal.

SULPHUROUS ACID. Sulphurous acid and the bisulphites are widely used for preserving foods. They act 1, by abolishing the oxygen and 2, by suspending the growth of moulds and ferments like those of the viscous, acetous, lactic and butyric fermentations. It has been used as a preservative for milk intended for butter and cheese making. It is used extensively in beer, wine and fruit syrups to absorb the oxygen and prevent secondary fermentations. Sulphurous acid is used by refiners of beers and making of lime juice and vinegars. It is also used in the preservation of meats. In canned goods it is objectionable as it may dissolve the lead and tin from the metallic envelopes.

Experimental. Fifteen minims of sulphurous acid were taken three times a day, *after* each meal for the period of one week. In this experiment five examinations of the normal urine were made twelve days before the drug was taken. In addition to the drug

period, seven examinations were made during the following week, making three series of examinations in this experiment.

URINARY TABLE

Normal Period	Amount	Sp. gr.	Solids	Chlorides	Sulphates	Phosphates	Urea
Apr. 13–17							
Average of							
5 Examinations	826	1022.6	45.22	13.48	1.38	1.87	21.73
Sulphurous Acid Period							
Apr. 29–May 5							
Average of							
7 Examinations	875	1026.8	53.43	14.71	1.75	2.33	27.90
After Period							
May 6–13							
Average of							
7 Examinations	757	1026.5	46.57	12.52	1.83	2.09	24.28
Maximum of							
Normal Period	980	1024.	47.92	15.98	1.60	2.23	24.70
Maximum of							
Drug Period	1150	1030.	59.41	21.95	2.33	3.01	33.10
Maximum of							
After Period	850	1030.	51.42	15.02	2.10	2.28	25.50
Minimum of							
Normal Period	800	1020.	44.27	9.48	1.20	1.57	19.20
Minimum of							
Drug Period	750	1020.	39.46	11.33	1.16	1.55	24.70
Minimum of							
After Period	650	1024.	44.72	9.85	1.60	1.98	22.10

A comparison of the averages shows that there was an increase of all constituents during the drug period as compared with the normal and that the after period corresponds more closely with the normal than the drug period, except in specific gravity and in the amount of sulphate which curiously enough, is in greater quantity than during either of the other periods. The increased elimination would indicate a greater metabolism.

ECHINACEA. This drug is obtained from the root of *Echinacea Angustifolia* and various claims are made for it. It is especially recommended in blood depravation and is useful in anemia. All

glandular organs are said to undergo a stimulating influence with increased functional activity. Digestion, absorption, assimilation, and general nutrition is improved. It is said to stimulate, markedly, retrograde metabolism, influence the lymphatic system and stimulate the capillary circulation.

This drug was experimented with for the purpose of determining its effect on metabolism. Five grains of the extract in tablet form were taken just before each meal.

URINARY TABLE.

Normal Period	Amount	Sp. gr.	Solids	Chlorides	Sulphates	Phosphates	Urea
Feb. 8–14 Average of 7 Examinations	873.5	1025.1	50.589	13.15	1.25	1.37	26.45
Echinacea Period Feb. 15–21 Average of 7 Examinations	907.	1024.8	51.97	13.18	1.16	1.61	21.51
Maximum of Normal Period	1140.	1030.	58.368	17.44	1.40	1.87	29.75
Maximum of Drug Period	1050.	1030.	63.52	15.93	1.57	2.52	31.50
Minimum of Normal Period	700.	1022.	47.50	10.47	1.10	0.68	23.80
Minimum of Drug Period	750.	1022.	45.37	11.94	0.75	1.14	16.50

A comparison of the averages shows that there was some diuresis and a slightly greater elimination of solids during the drug period, except in sulphates and urea. The difference in the latter is quite marked and is contrary to the results of some other investigators. (19).

The drug appeared to act as a tonic ; increased the appetite considerably and appeared to give better tone to the system generally.

BIBLIOGRAPHY.

1. Rideal S. Disinfectants and Preservatives, 1903.
2. Lancet. Dec. 20, 1879.
3. Journal of Franklin Institute, Dec., 1898.
4. Journal of Physiology, 1898.
5. Hyg. Congress. Geneva, 1882, II. 352.
6. Bulletin 86. Maryland Experiment Station.
7. Cornell Expt. Sta. Report 1899–1900.
8. Journal of Franklin Institute, 1899, Vol. 147.
9. American Jour. Physiol, 1898, Vol. I.
10. British Medical Journal, 1889.
11. Zentralblatt für innere Medizin, 1903.
12. Jour. Med. Ass'n, 1903, Vol. 40.
13. Hygiene Rundschau, 1902.
14. Archive Expt. Path., 1881, Vol. XIII, p. 175.
15. Klebs Archives Vol. VIII, p. 140.
16. Archive Ginirale de Medicine, 1874, Vol. XXIV, p. 566.
17. Dorpot Essays, 1880.
18. Philadelpeia Medical Journal, 1900, Vol. V, p. 456.
19. P. A. Fish. American Veterinary Review, 1903, Vol. XXVII.

Compliments of
PIERRE A. FISH.

ABSTRACTS

OF

WORK DONE IN THE LABORATORY

OF

VETERINARY PHYSIOLOGY AND . . . . PHARMACOLOGY . . . .

UNDER THE DIRECTION OF P. A. FISH

NO. 3

NEW YORK STATE VETERINARY COLLEGE
CORNELL UNIVERSITY
ITHACA, N. Y.
1906

TABLE OF CONTENTS

URETHRAL CALCULUS IN THE DOG.

PIERRE A. FISH.

The patient, a male coach dog, four years of age, weighing about fifty pounds was brought to the clinic*, May 1, 1905. The history, as given by the owner, was to the effect that the dog appeared to be in a normal condition up to within about 24 hours of the time that he reach the clinic. Attempts at micturition were unsuccessful although the animal used his best efforts.

An examination of the urethral tract was made externally and a small movable mass was detected at the proximal end of the bone of the penis. A small sized catheter was also passed but met an obstruction, easily distinguished by a peculiar grating sound and by the fact that the catheter would go no farther. The use of the catheter confirmed the external examination and as it was quite evident that the mass could not be forced out through the urethra, the patient was prepared for an operation.

Anesthesia was effected by the injection of one half grain of morphine sulphate hypodermically and the inhalation of ether. The operative area was shaved, disinfected and a longitudinal incision was made on the left side of the sheath at the proximal end of the penal bone. The cut was continued through the urethra directly to the obstruction and a calculus of irregular form and about the size of a small pea was removed.

It was planned to draw the accumulated urine from the bladder with a catheter after the calculus was removed, but before this could be accomplished, the patient passed a considerable quantity of urine without assistance, through the urethral incision. The wound was disinfected with sublimate solution and the urethral incision sutured with catgut ; the dermal incision was also loosely sutured with the same material.

*N. Y. State Veterinary College.

The following day the stitches were removed from the external wound and some clots of blood removed. The sheath and testicles were considerably swollen. Thermofuge was applied locally and eight grains of Ichthyol were given internally three times a day to relieve the inflammation. Urination occured in a normal manner except that the urine last expelled was of a bloody character. The wound was dressed daily with sublimate solution and dusted with compound alum powder. The swelling of the sheath soon yielded to the treatment, but the orchitis continued. After a few days more of the same treatment, this condition also improved. The temperature hung about 103°. The highest temperature recorded was 103.8°.

Two weeks after the operation, 5 grains of Sodium Benzoate were administered three times daily and the Ichthyol discontinued. The dog was discharged May 16, and the owner advised to continue the Sodium Benzoate and to dress the wound, which was not quite healed, with the sublimate solution.

On June 10, the dog was returned with symptoms similar to those exhibited May 1. The dog could pass only a few drops of urine at a time. The catheter showed an obstruction at the base of the bone of the penis as before. An operation was immediately performed similar to that of May 1, except that the incision was made upon the right side of the sheath. The calculus this time was not much more than half as large as the previous one, and with it came a still smaller one. In both operations, there were in addition to the larger calculi a few smaller ones of about the size of a pin head.

In this operation the urine was not passed through the wound as before and there was doubtless less infection, because there was scarcely any swelling of the sheath and the wound appeared to be in a healthy condition. There was some orchitis, however, which gradually improved without special treatment. The procedure and treatment in the second operation were very similar to that of the first, except that Ichthyol was given for a shorter period and a tablet of Calcalith three times a day was substituted for the Sodium Benzoate. The Calcalith (a combination of Calcium, Lithium and

Colchicine) was given with the idea of its forming combinations with the phosphates and eliminating them through the intestinal canal thereby decreasing the elimination through the kidneys.

Shortly after the first operation the urine was examined for phosphates and the normal amount was found to be more than doubled. A partial analysis of the calculus was made. Phosphates and carbonates were found to be present, probably in combination with lime as a base. For three months there was no return of the trouble and the owner reported the dog to be in as apparently a normal condition as ever.

On September 13, the dog was returned by the owner. (The dog was exhibited at the State Meeting, then in session). There was considerable orchitis and swelling of the sheath. On the left side of the sheath near the scrotum there was an opening in the skin from one to two centimeters in diameter. It appeared as if some urine escaped through this orifice, but an attempt to pass a catheter through it was not successful. An attempt to pass the catheter through the penis was likewise unsuccessful at first, although it was passed later. The swollen condition of the parts made an external examination for calculus very difficult.

The dog was placed under morphine-ether anesthesia and the skin orifice enlarged and the incision carried down to the urethra. A catheter was easily passed through this orifice into the bladder. A catheter was also passed the full length of the penis without obstruction, indicating that no calculus was present in the urethra and probably no stricture. The wound was dressed antiseptically but not sewed.

On the day after the operation, there was no trouble in passing a catheter and drawing some of the urine. A small opening now appeared in the skin upon the right side of fhe sheath as if there might be pus present, although none was seen. Temperature 101°. The wound was dressed and injected with Compound Iodine Solution (Lugol's). The swelling of the sheath soon decreased as did that of the scrotum, although more slowly. The urine at first passed through the wound but on the sixth day after the operation it was observed to pass normally through the penis.

Within two weeks the swelling and orchitis had disappeared and the wound was healing nicely; but at this time the dog was not feeling so lively as heretofore and soon gave evidences of sickness by refusing his feed and developing a slight rise in temperature. The treatment consisted of tonics and antipyretics without much apparent change in his condition. Although not improved in health, he was taken home by the owner after the third week and the treatment kept up. The dog, however, grew weaker, and two weeks after he was taken home he wandered away and never returned. It is much to be regretted that an autopsy could not have been held.

It was brought out later, that just previous to the last attack the owner had washed the dog in a creek and he believed that the dog had taken cold at this time. The swelling of the sheath and scrotum may have been caused by this cold bath, as the tissues in the above named parts were probably weakened from the previous operations and therefore more susceptible—the effect ultimately extending through the whole system and being more or less responsible for the fatal ending, notwithstanding the fact that the wounds were healing nicely and that the surgical part of the case was apparently successful.

There is some variance in opinion as to the frequency and treatment of such cases as shown by the following extracts:

Ashmont (Joseph F. Perry, Jr.), "Dogs: Their Management and Treatment in Disease" (1886), states regarding cystic calculi that "a cure is out of the question" and that "the symptons must indicate the line of treatment to be followed."

J. H. Steel, "A Treatise of the Diseases of the Dog" (1888), states that cystic calculi must be considered as frequent in the dog, and that cases are also on record in the bitch. With regard to the urethral calculus he says this "is generally a small cystic stone impacted in its passage (urethra). Manipulation may enable us to bring it down to the orifice of the canal and there grasp it with the forceps and so afford relief, otherwise an incision must be made on it, where it can be felt in the urethra, and removal so effected."

J. Woodroffe Hill, "The Management and Diseases of the Dog" (1900, 5th Edition), states that in June, 1881, he performed the first recorded case in English literature of canine lithotomy on a St. Bernard bitch.

Müller, "Diseases of the Dog" translated by Glass, recognizes four types of urinary calculi: urates, oxalates, phosphates and cystic stones. The latter being soft, wax-like bodies with a shiny, crystalline, irregular surface. The composition of the other types is indicated by the names. He also reports a calculus weighing 490 grams (about one pound) having been taken from a German boar-hound.

The origin of the calculi is generally in the pelvis of the kidney, according to Müller, usually from some foreign body, as a blood clot, a piece of mucus, epithelium, etc., around which the sediment in the urine forms and gradually the crystalline elements accumulate. This deposit is especially favored in cases of cystitis, where the urine is undergoing alkaline fermentation and produces a copious sediment in the urine. Where there is ischuria (retention or suppression of urine) relief by operation or drawing off the urine must be reasonably prompt. If the urine is not drawn off in three days the bladder is ruptured and it may burst in two days. When the rupture occurs, death takes place in a few hours.

Müller states that it is well established that it is impossible to produce any good results from the injection into the bladder of any of the various agents that are supposed to have the property of dissolving calculi; as for instance acids for dissolving phosphatic calculi, alkalies for breaking up uric calculi, or the drinking of mineral waters, such as Vichy, Wildung, Carlsbad. He recommends the operation of urethrotomy if the calculus is located in the urethra, or cystotomy if located in the bladder.

In his operation in urethrotomy, he recommends that the wound be left open unless it be large, in which case only one stitch is employed. The urine escapes through the wound for two days, but the wound soon closes, and in eight or ten days, he states, the urine is passed in the natural way.

Frederick T. G. Hobday, "Surgical Diseases of the Dog and Cat" 2d Edition. 1906. In the dog and cat, particularly in the male animals, small calculi are frequently met with in the urethral canal.

In one instance Dr. Hobday removed eleven calculi at one urethrotomy operation, the patient being a St. Bernard dog. On each of two other occasions he counted more than fifty small calculi in the urethra aud bladder. Relief from distended bladder due to calculi may be obtained either by puncture of the bladder or urethrotomy. In the former case a trocar and cannula, with due antiseptic precautions, are inserted into the bladder through the linea alba from 1 to 3 inches behind the brim of the pelvis, so as to pierce the bladder where it is tense and fairly close to the neck. One patient was operated upon in this way five times in three months with no bad results.

The operation for urethrotomy is to remove the stone. Dr. Hodbay recommends an incision in the median line directly over the calculus and the stone removed with any others within reach, and the parts thoroughly washed with a fluid antiseptic. In some cases he thinks it wise to leave the catheter *in situ* for some hours after the operation. If the wound is small he recommends suturing and covering with Iodoform and Collodion ; but if of some length, a small orifice should be left for drainage, as otherwise the urine will find its way through and disturb all the sutures. In any case it does not much matter, and many operators advise using no sutures at all, but treating the place as an open wound. In the female the shorter urethral canal does not offer quite so many difficulties.

"The *Prognosis* of these cases is excellent except where the patient has been left until almost in a state of collapse before surgical aid is attempted. The internal administration of bladder and urethral sedatives, such as urotropin, hyoscyamus, buchu, pearl-barley-water, etc., afterwards are useful aids to convalescence. The chief dangers in the future are those of stricture or the presence of another stone which may escape from the bladder."

ARECOLINE HYDROBROMATE.

HOWARD J. MILKS, WATERTOWN, N. Y.

Arecoline is the alkaloid of Areca nut. The nut has been for a long time in use as a remedy for tapeworms and other worms of the intestinal tract. The alkaloid has been employed as an active purgative in colic and laminitis. It is claimed that it is more active as a purgative than eserine or pilocarpine or both. It is also said to be a remedy for tapeworms and has been used for its effects upon the eye as a myotic. Before beginning a description of its properties, some references may be noted as to the characteristics of the drug.

U. S. Dispensatory. Areca nut, or Betel nut as it is sometimes called, is the product of an East Indian tree belonging to the family of palms. The fruit, which is about the size and shape of a small egg, and of an orange color, contains the nut imbedded in a fibrous fleshy envelope, and invested with a brittle shell which adheres to the exterior flesh.

The Betel nut of commerce is of a roundish conical shape, rather larger than a chestnut, externally of a deep brown, diversified with a fawn color, internally brownish red, with whitish veins, very hard, of a feeble odor when broken and of an astringent taste. It abounds in tannin and also contains gallic acid, a fixed oil, gum, a little volatile oil, lignin and various saline substances.

E. Bombalon obtained from it a volatile alkaloid, resembling nicotine, which he named Arecaine. It is left from an ethereal solution in the form of a colorless, oily liquid smelling like weak meat broth and having a strong alkaline reaction.

With tartaric, citric, hydriodic and salicylic acids it forms varnish like salts, the salicylate having a tobacco-like odor. Its taste is, at first, imperceptible but later acrid. It increases the secretion of saliva, lessons the pulse and has a purgative action.

E. Jähns has found three alkaloids: Arecoline $C_8 H_{13} NO_2$, identical with the Arecaine of Bombalon, Arecaine $C_7H_{11}NO_2+H_2O$ which occurs in colorless crystals, permanent in the air, soluble in water but not in absolute alcohol, chloroform, ether or benzol; thirdly an alkaloid which exists in quantities too minute to analyze.

Jähns considered Arecaine the active principle and pronounced it a powerful teniacide resembling Pelletierine. It also resembles Muscarine but depresses both the heart and respiration; causes tetanic convulsions and increases peristalsis extraordinarily. It contracts the pupil.

Arecoline is a volatile oil, miscible in all proportions in water, alcohol, ether and chloroform, forms crystalline salts and is pronounced very toxic. It exists in the nut in the proportion of 0.1%. The hydrobromate is the form in which it is used: The dose for the horse being one-half to one grain. It is a more powerful stimulant of the salivary glands than Physostigma and is especially used in colics in horses in the above doses and for tapeworm in man in 1-15—1-10 grain doses. It is also used as a myotic. A 1% solution in the eye produces strong myosis. It has been pronounced superior to Physostigma in glaucoma, though less enduring in effect.

E. Fröhner finds that it increases secretions and peristalis acting similarly to a combination of eserine and pilocarpine. The first passage from the intestines takes place in from one fourth to one half hour after the injection. The laxative effect is followed by slight colicy symptoms. Large doses are diaphoretic. Poisonous doses bring about an irregular condition of the heart, lessen blood pressure and slows the heart. Five grains kills a horse. As a therapeutic agent he has employed it on account of its action, stability of preparation and cheapness. It has proven valuable in colic and laminites.

Dr. W. L. Bell recommends its use in colic and laminitis. The treatment in laminitis consists of injecting one grain daily subcutem, along with applications to the feet. He states that before using Arecoline he could not get such good results although the other parts of the treatment were as rigidly adhered to.

A Belgian veterinarian reports a series of cases of laminitis in which recovery took place very promptly. The animals were fully recovered and put to work on an average of about six days.

I have experimented upon several dogs to ascertain the effects of the drug in different doses.

Case No. 1. Fox Terrier weighing 18 lbs. One half grain of Arecoline Hydrobromate was administered subcutaneously. In three minutes he was dull and weak. He leaned against the cage, then pitched headlong to the floor. He was thrown into convulsions at each attempt to move. In a short time he was quiet, lying upon his side; his breathing was irregular and his mouth was wide open. At times his breathing was labored and difficult, then quiet as if in deep sleep. The pupils were dilated. The bowels moved in fifteen minutes and again in one and a half hours.

Case No. 2. Weight about 25 lbs. The doses were given on alternate days, beginning with 1-20 grain. This had no effect except to accelerate the breathing. A dose of 1-10 grain produced salivation and passages from the bowels in 1½ hours. Upon giving a dose of 1 grain the bowels moved twice very copiously within eight minutes. The pupils were dilated. The animal was weak, depressed, breathing irregular and he layed upon his side with legs extended. The following day the dog was as well as usual. Upon giving a dose of 2 grains, the feces were passed in six minutes, also the urine. Another passage of feces in five minutes. He was very weak and irritable. The pupils were dilated and he rested upon his side. There was a third passage of feces in ten minutes. In one hour he was resting easily and took note of his surroundings. The next morning he was better but would not eat. The bowels were still loose and blood was passed with the feces. He gradually grew better for the following six days, when he had apparently recovered. Later he was given 3 grains with essentially the same symptoms as were secured with the former dose, except that they were more severe. He was injected at 2:30 P. M. and died the following morning at 9 A. M.

The post mortem showed: lungs normal; spleen slightly congested; stomach full of a dark green liquid. The small intestines

were congested in areas ½-2 inches long. Cecum congested. Liver, pancreas and kidneys normal. Bladder congested. Auricles empty. Ventricles full of dark blood. The mucosa of the ileum was very much congested and showed a bloody exudate. The contents of the intestine were bloody. Seven tapeworms were found in the small intestines. This fact was interesting, since the dog had been repeatedly dosed with the drug and in quantity sufficiently to purge and finally to kill, yet the worms had not been expelled.

Several kittens were used. Doses of ⅛ to ½ grain proved toxic with the following symptoms: Feces in about three minutes. Signs of illusions. Ran about cage with tail bristled and spitting at imaginary objects. Very irritable. Pupils dilated. Lying upon its side in 8 to 10 minutes. Soon the respirations ceased but the heart did not stop until one or two minutes later. A dose of 1-16 grain produced no symptoms in a cat of 5 or 6 pounds.

To test the keeping qualities of the solution, one fifth grain that had been in solution for two weeks was injected. This seemed as powerful as a fresh solution, killing the cat in a few minutes and with the usual symptoms.

In a dog under chloroform anesthesia, $\frac{1}{12}$ grain was injected into a loop of the intestine and the loop ligated at either end. An adjacent loop was kept as a control. In three fourths of an hour the different segments were examined. The segment receiving the arecoline appeared harder and firmer than the control. Upon cutting open both segments, congestion was found in the one containing the arecoline but not in the other. No difference in the amount of secretion could be noticed. Salivation did not occur. In each segment living tapeworms were found.

To try the effect of the drug upon the heart, experiments were performed upon the horse and frog. In the case of the former, intravenous injections were used and a blood pressure tracing taken. In each case a very rapid fall in blood pressure was obtained. In the case of the frog a minim of the solution was dropped upon the heart. It was found that 1% would stop the heart within one beat and more permanently than stimulation of the vagus. Solutions of 0.1% acted nearly as strongly as the 1%. If a drop of strychnine or

atropine solution were applied before the arecoline, the action of the drug was not very marked.

As a curative agent, I have not had much opportunity for experiments. In one case of impaction colic in a mare possessing an enormous ventral hernia, I gave ½ grain and secured no action other than salivation. Half an hour later ¾ grain was given and a copious discharge was secured from the bowels in about 20 minutes.

The salivation was very marked. In about ten minutes the animal opened its mouth and a mouthful of saliva fell out. The saliva kept dropping for about 15 or 20 minutes. During the action of the drug the animal was quite restless and colicy.

In one stable in which laminitis occured at the same time, arecoline was given to two horses and an aloes ball to the third; in other respects the treatment was the same. The two receiving the arecoline were worked on the second day and were examined in the evening. They were found entirely recovered. The third case also worked on the second day but was pretty sore at the time of examination.

The following conclusions as to the action and uses of arecoline may be drawn from the preceding experiments and the literature upon the subject; that it is a rapid intestinal evacuant, increasing both peristalsis and the secretions. That its action is accompanied by colicy symptoms and profuse salivation. That its action upon the eye is two-fold, locally it is a myotic and internally a mydriatic. That the chief dangers in its use are on account of its action upon the heart and respiration.

Indications for its use are in cases of colic, laminitis or wherever a rapid evacuant is desired.

That as a remedy for worms, especially as a teniacide, it cannot be relied upon from the facts that solutions of it have failed to expel the worms when given in doses sufficient to produce purgation and finally to kill the dog, nor did the solution kill the worms applied to them directly, as in the case where the bowel was ligated.

Its chief advantages over eserine and pilocarpine are that it is more permanent in solution, and is cheaper especially if purchased in bulk.

THE EFFECTS OF SULPHUROUS ACID UPON PEPTIC AND TRYPTIC DIGESTION.

PIERRE A. FISH.

The more closely digestion experiments can be made to approximate normal conditions the more reliable they are. Normally the digestive products are absorbed soon after they are formed. In test tube experiments no absorption occurs and the accumulation of the digestive products may interfere with the complete digestion of the food stuff.

In the following experiments the sulphurous acid was, in most instances, added to the artificial digestive fluids at the same time the substances to be digested were added. Possible explanations for negative results would be that the acid might have an inhibitory action upon the enzyme, or change the constitution of the food stuff, or both effects might occur coincidently.

EXPERIMENT I. A solution was prepared by dissolving 1 centigram of scale pepsin in 100 cc of a 0.2% solution of hydrochloric acid. Tube 1 served as control and contained 1 gram of dry fibrin in 20 cc of the above fluid. Four more tubes were prepared in the same way; but varying proportions of sulphurous acid were added. Tube 2 contained 1 minim; tube 3, 2 minims; tube 4, 5 minims and tube 5, 10 minims of sulphurous acid. All of the tubes were placed in the incubator for 24 hours at a temperature of about 40° C. Very good tests were obtained from all of the tubes showing the presence of soluble and acid albumin, albumose and peptone. The undissolved residues were dried to constant weight and the weight taken to determine the amount of the substance which had gone into solution as shown in the following table:

	Dried Residue.	Percentage Dissolved.
Tube 1, Control	17.50%	82.50
" 2, 1 miuim H_2SO_3	18.00%	82.00
" 3, 2 " "	10.20%	89.80
" 4, 5 " "	16.90%	83.10
" 5, 10 " "	20.70%	79.30

Tube 3, with the greatest solubility, gave the least satisfactory peptone test; while tube 5 with the least solubility gave a good peptone test.

EXPERIMENT II. 3.35 milligrams of scale pepsin were dissolved in 100 cc of 0.2% hydrochloric acid. The whites of freshly boiled eggs were passed through a number 40 sieve. Ten grams of this finely divided albumin were placed in flask 1 with 30 cc of the above solution. Flask 2 was prepared in the same way except that 10 minims of the undiluted sulphurous acid were added. Both flasks were placed in the incubator at 40° C for 48 hours.

	Dried Residue.	Percentage Dissolved
Flask 1, Control	6.25%	93.75
" 2, 10 minims $H_2 SO_3$	9.78%	90.22

Peptones were found in both flasks, but No. 1 was more satisfactory. A greater part of the albumin also went into a solution.

EXPERIMENT III. A pepsin solution similar in strength to Experiment II was used. Two grams of finely divided lean meat were used in each flask in this experiment.

Flask 1, Control — Meat. + 30 cc of pepsin solution.
" 2, 5 minims $H_2 SO_3$ — " " " " "
" 3, 5 minims $H_2 SO_3$ — " " " " "
" 4, 2 gms. meat placed in 30 cc of undiluted $H_2 SO_3$ for 48 hours. After draining it was put in 30 cc of the pepsin solution.
" 5, Same as No. 4, except that after draining it was fried in a spider with a little lard for a few minutes. It was then placed in 30 cc of the pepsin solution.
" 6, 2 gms. of normal fresh meat fried in spider as No. 5. Then placed in 30 cc of the pepsin solution.

All flasks were placed in the incubator at 40° C and digestion allowed to continue for 48 hours.

	Dried Residue.	Percentage Dissolved.
Flask 1, Control	10.00%	90.00
" 2, 5 minims $H_2 SO_3$	10.65%	89.35
" 3, 5 minims $H_2 SO_3$	11.10%	88.90
" 4, undiluted $H_2 SO_3$	15.50%	84.50
" 5, $H_2 SO_3$ cooked	23.95%	76.05
" 6, normal, cooked	45.80%	54.20

Soluble albumin, acid albumin, albumose and peptone were found in all the flasks; the least satisfactory peptone test being obtained from flask 5. No. 6 gave marked peptone tests but was poorest in solubility. Cooking very evidently retards solution of the meat.

Experiment IV. The pepsin solution consisted of 2 centigrams of scale pepsin in 100 cc of 0.2% hydrochloric acid.

Tube	1,	a bit of	fibrin	+ 30 cc	of pepsin	solution				
"	2,	"	"	"	"	"	"	+ 4	minims	H_2SO_3
"	3,	"	"	"	"	"	"	+ 8	"	H_2SO_3
"	4,	"	"	"	"	"	"	+ 15	"	H_2SO_3
"	5,	"	"	"	"	"	"	+ 30	"	H_2SO_3
"	6,	"	"	"	"	"	"	+ 45	"	H_2SO_3
"	7,	"	"	"	"	"	"	+ 60	"	H_2SO_3

The temperature of the contents of the tubes, at the beginning of the experiment was 30° C; this was raised to 40° C and digestion continued for two hours. At the end of that period, peptones and all of the intermediate products were found in all of the tubes. In tubes Nos. 1 and 2 the reactions did not appear to be as strong as in the remaining tubes.

Experiment V. One centigram of scale pepsin was dissolved in 100 cc of undiluted sulphurous acid. In 20 cc of this solution was placed a half gram of fibrin in a moist condition. Digestion proceeded for 24 hours. Good peptone tests were obtained. There was not the usual swelling and translucency of the fibrin as when hydrochloric acid was present. The fibrin remained opaque; digestion occurred by erosion with slow disintegration of the mass.

Experiment VI. An artificial digestive fluid was made by macerating a portion of the mucous membrane of the stomach of a cat in chloroform water. The extract was filtered and 1 part of it was added to 9 cc of 0.2% hydrochloric acid for the digesting fluid in each tube. Three tubes were used: No. 1 containining 1 gram of fibrin which had previously been soaked in water for 4 hours, and then allowed to dry again. No. 2 was treated similarly to No. 1 except that the fibrin was soaked in a solution consisting of sulphurous acid 1 cc, water 29 cc, for 4 hours. No. 3 was the same as No. 2 except that the fibrin was immersed for 4 hours in undiluted

sulphurous acid. Digestion was allowed to go on for about 10 hours at the usual temperature. Peptones and all of the intermediate products were found. In No. 3 the fibrin had practically all disappeared: in No. 2 there was but little, while in No. 3 there was the largest amount of fibrin. The sulphurous acid had apparently increased the solubility of the fibrin.

EXPERIMENT VII. Each flask contained 2 grams of broiled beef finely divided, immersed in 30 cc of a 0.1% solution of pepsin in the usual percentage of hydrochloric acid. Flask No. 1 served as control and was prepared as above described. Flask No. 2 was similar except that previous to broiling the meat had been preserved by immersion for a few hours in a 2%* solution of sulphurous acid. In flask No. 3, the meat had been preserved in a 5% and in No. 4 a 10% solution of sulphurous acid. Digestion proceeded for 24 hours.

	Dried Residue.	Percentage Dissolved.
Flask 1, Control	19.10%	80.90
" 2, 2% preservative	16.85%	83.15
" 3, 5%	16.95%	83.05
" 4, 10%	14.15%	85.85

Digestion had apparently been very thorough as all of the flasks gave excellent tests for albumoses and pepsin.

TRYPTIC DIGESTION.

EXPERIMENT VIII. Five hundred milligrams of trypsin were dissolved in 123 cc of 1% sodium carbonate. Flask 1 contained 2 grams of finely divided raw beef in 30 cc of the trypsin solution and 30 cc of water. Flask 2 was similar to No. 1 except that 5 minims of sulphurous acid were added. Flask 1a similar to No. 1 except in the amount of the trypsin solution and water. This flask contained in addition to the meat 60 cc of the trypsin solution and 60 cc of water. Flask 2a was prepared similarly to 1a but with the addition of 10 minims of sulphurous acid.

*These figures do not refer to the amount of absolute acid, but to the percentage of the commercial solution dissolved in water.

	Dried Residue.	Percentage Dissolved.
Flask 1, Control	12.40%	87.60
" 2, 5 minims H_2SO_3	14.65%	85.35
" 1a, Control	15.95%	84.05
" 2a, 10 minims H_2SO_3	14.50%	85.50

Digestion continued for 48 hours. Flask 1 gave a slight indol reaction and only faint traces of albumose and peptone. Flask 2 gave neither indol nor albumose nor peptone reactions. Flask 1a gave only a trace of albumose and a fair test for peptone. Indol was absent. Flask 2 a, indol absent. Traces of albumose and peptone. The sulphurous acid restrained putrefactive processes as shown by the absence of indol in Nos. 2 and 2a.

Experiment ix. This experiment was similar to No. vii in peptic digestion. The trypsin solution was the same as used in No. viii. Flask No. 1 was control and contained 2 grams of broiled beef, finely divided, with 30 cc of the trypsin solution. Flask No. 2 was similar except that previous to broiling the meat had been preserved by a few hours immersion in 2% sulphurous acid. In flask No. 3, a 5% and in No. 4, a 10% solution of sulphurous acid was used to preserve the meat. Digestion continued for 24 hours at 40°C.

	Dried Residue.	Percentage Dissolved.
Flask 1, Control	25.70%	74.30
" 2, 2% preservative	26.60%	73.40
" 3, 5% "	20.00%	80.00
" 4, 10% "	17.90%	82.10

All the flasks showed good peptone tests; they also showed indol.

Experiment x. The solution was prepared by dissolving 0.28 gram of pancreatin in 100 cc of a 1% solution of sodium carbonate. Flask 1 contained 2 grams of finely divided raw meat in 30 cc of the above solution and 30 cc of distilled water. Flask 2, the same with the addition of 5 minims of sulphurous acid. Flask 1a contained 2 grams of finely divided raw meat in 60 cc of the pancreatin solution and 60 cc of water. Flask 2a, the same as 1a with the addition of 10 minims of sulphurous acid.

	Dried Residue.	Percentage Dissolved.
Flask 1, Control	18.50%	81.50
" 2, 5 minims $H_2 SO_3$	18.05%	81.95
" 1a, Control	22.35%	77.65
" 2a, 10 minims $H_2 SO_3$	14.85%	85.15

No indol was found in any of the flasks. Very faint tests for peptones were obtained from all but No. 2. Alkali albumin and albumose were found in all. Digestion occurred for 24 hours at 40°C.

Experiment xi. This experiment was in line with Nos. vii and ix. The pancreatin solution being the same as in No. x. Flask No. 1 was Control and contained 2 grams of broiled beef. finely divided, and 30 cc of the pancreatin solution. Flask No. 2 was similar except that previous to broiling the meat had been preserved by a few hours immersion in 2% sulphurous acid. In flask No. 3, a 5%, and in No. 4, a 10% solution of sulphurous acid was used to preserve the meat. Digestion proceeded 24 hours at 40°C. Peptones and intermediate products were found in all of the flasks.

	Dried Residue.	Percentage Dissolved.
Flask 1, Control	40.35%	59.65
" 2, 2% preservative	31.05%	68.95
" 3, 5% "	31.50%	68.50
" 4, 10% "	30.10%	69.90

This series gives a lower percentage of solubility than any hitherto encountered, but as in the case of the pepsin and trypsin experiments the solubility is in favor of the acid treated meat, No. 3 gave a pronounced test for indol; in No. 2 there was a suspicious trace but it was entirely absent from Nos. 1 and 4.

Experiment xii. A 0.2% solution of pancreatin was prepared by adding 0.5 gram of pancreatin to 250 cc of 1% sodium carbonate. The solution was quite turbid and filtration did not remove the turbidity completely.

Tube 1,	a bit of fibrin + 20 cc pancreatin solution.	Control.		
" 2,	" " " " " "	+ 15	minims	$H_2 SO_3$
" 3,	" " " " " "	+ 30	"	"
" 4,	" " " " " "	+ 60	"	"
" 5,	" " " " " "	+ 90	"	"
" 6,	" " " " " "	+ 120	"	"

Digestion was allowed to proceed for 50 or 60 hours at 40° C. The addition of the acid would neutralize a certain amount of the alkali of the pancreatin solution. The first three tubes gave an alkaline reaction. Tube 4 was near the neutral point but weakly alkaline. Tubes 5 and 6 were distinctly acid. No 1 showed the presence of alkali albumin and a slight amount of albumose and peptone. None of the other tubes showed any signs of albumose or peptone. Nos. 2 and 3 showed alkali albumin. No 4 only a trace of the alkali albumin; while Nos. 5 and 6 showed no evidence whatever of digestion.

EXPERIMENT XIII. As meat contains a considerable percentage of water, it seemed desirable, in connection with the experiments, to determine this percentage. Two grams of fresh raw beef were finely divided and dried to constant weight. The dry residue weighed 0.612 gram; or the original 2 grams of meat consisted of 30.60 % dry material and 60.40 % of fluid. In the majority of the experiments the percentage of dry residue was less than in this case, showing that some of the material must have actually dissolved. In experiment xi, however, the percentage of dried residues is greater; nevertheless, good peptone tests showed that digestion had occurred. The cooking of the meat would also retard any tendency to dissolve.

CONCLUSIONS.

In peptic digestion a slightly greater percentage of solubility was obtained from the controls in the case of raw meat and boiled egg, where the normal percentage of fluid is rather high. In the tryptic digestion of raw meat the evidence was more favorable to the preparations containing a slight amount of sulphurous acid.

In both peptic and tryptic digestion the evidence was uniformly in favor of the meat preserved in the acid before cooking. This was true of fibrin as well as meat.

The development of peptone was not necessarily correlative with the solubility of the substance. In some instances where there was great solubility there were poor or negative peptone tests,

while in other cases with a low percentage of solubility excellent peptones were obtained.

Peptic digestion was retarded but not checked by substituting undiluted sulphurous for the normal 0.2% hydrochloric acid.

Peptones apparently develop as quickly in the acid preparations as in the controls.

In tryptic digestion sulphurous acid completely checks action if enough of it be added to render the medium acid. Small amounts of the acid with the medium still alkaline do not apparently interfere with digestion.

ERGOT AS AN ABORTIFACIENT.

ARTHUR J. BURLEY, ANGOLA, N. Y.

HISTORICAL.

The medicinal uses of ergot date back some centuries. Some of the earliest references during the sixteen century, show that some of its virtues were already known to the masses, and that it was used extensively in obstetric practice. Numerous epidemics due to ergot are reported during the eighteenth century. Salerne proved the poisonous effects of ergot on pigs, ducks and fowls ; the animals dying of gangrene. He corroborated the statement that the fresh ergot was the most virulent and that, after some months it sweated and lost its poisonous properties.

Allusions to ergot were quite numerous during the eighteenth century, it being used mainly by the lower classes and by charlatans with criminal intent. In France, its use was interdicted in 1774. Its reputation declined but was later revived by the efforts of American physicians. Drs. Stearns, 1807, Akerly, Prescott 1813, Chapman, Dewees (1817–1818) and Altee in 1821 largely contributed to turn the tide in its favor. European physicians combated the idea of its efficiency, but ergot was finally admitted to the London Pharmacopocia in 1836.

PHYSIOLOGIC ACTION.

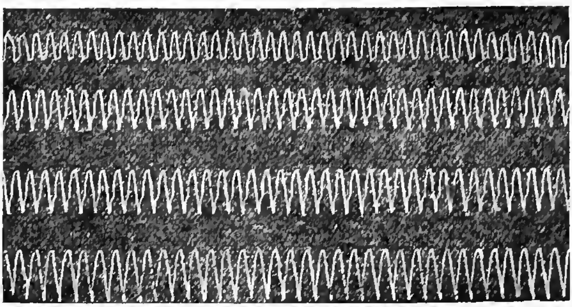
Digestive System.—In large doses ergot is a gastro-intestinal irritant, occasioning considerable heat and dryness of the throat, accompanied by thirst and succeeded by pain in the stomach and bowels, vomiting and occasional purging, with violent peristalsis, although constipation is the common sequence.

Circulatory System.—Repeated medicinal doses increase the blood pressure, although rendering the pulse slower and smaller, the result primarily of stimulation of the vaso-motor center, followed

by peripheral action causing a tonic contraction of the small unstriped muscle fibers.

A poisonous dose lowers arterial tension, causing the pulse to beat faster and softer—an effect due to the exhaustion from over-stimulation or to direct depressant action upon the heart muscle. It is claimed by competent authority that there is no active and actual contraction of the arteries as a result of stimulation of the vaso-motor system, but that the arteries contract because of the fullness of the veins, there not being sufficient blood to fill both systems—marked arterial anemia resulting. Some difference of opinion exists as to the effects upon the circulatory system.

Experiments by the writer on the heart of a frog show that the force of the contraction is increased.



The first line is a tracing from the normal heart beat of the frog. The following tracings are from the same specimen after the application of ergot.

It is claimed by Willebrand that the normal or hypertrophied heart so contracts under the action of ergot that the difference in size is appreciable by percussion. No specific effects upon the blood have been described.

Nervous System.—Medicinal doses have no especial action though excessive doses sometimes depress the sensory mechanism producing general cutaneous anesthesia. Among the physiologic effects of toxic doses is stimulation of the organic motor centers.

Respiratory System.—Medicinal doses produce no particular effect. Large doses depress the respiratory center rendering the breathing shallow. This action is manifest from the first there

being no primary stimulation of the respiration. Death from an overdose of ergot usually results from paralysis of the respiratory center.

TEMPERATURE.—No special action has been observed. Toxic doses cause cold skin; the limbs, ears, horns and tail lose their natural warmth.

EYE.—The caliber of the retinal and nutrient optic blood vessels is reduced resulting in marked pallor of the disk, transitory amblyopia and papillary anemia.

UTERUS.—In some respects the most important action of ergot is upon this organ. Except in labor no appreciable effects are produced by very small doses although large doses are said to produce contraction. In therapeutic doses the principal action of the drug is on unstriped muscle fibers. It causes especially the contraction of the blood vessels and contraction of the uterus. Its action is most strikingly exemplified during pregnancy. It produces, in full doses, tetanic, tonic contraction of the uterine muscle, the uterus being hard and pale, forcing the blood out of the uterine arterioles.

The uterine contractions are attributed, in part, to stimulation of the parturition center in the lumbar portion of the cord. The precise manner in which ergot affects the uterus is still a matter of discussion. It is fairly well demonstrated, however, that the drug acts both centrally and peripherally owing to its different constituents, cornutin acting centrally and sclerotic acid peripherally.

Ergot has been studied as much or more than any drug in the materia medica and if opinions vary as to its *modus operandi*, it is because a very complex substance is dealt with, the nature and even the number of its constituents being as yet inadequately known. Some of the principles of the drug are unstable, and variable in their influence. Tanret's ergotinine, for example, is said to be without effect upon the uterus. Bonjean's ergotin is a powerful ecbolic and has marked action, moreover, upon the vascular system.

BLADDER.—In animals poisoned with ergot, the bladder may be found distended with urine or empty and firmly contracted. In the first instance there is a spasmodic contraction of the vesical

sphincter ; while in the latter case the entire muscular structure of the organ is under the influence of ergot. Peton noticed soon after an injection of ergot the appearance of fibrillary contractions resulting in the complete evacuation of the organ ; in other cases the contractions alone were seen. Wernich observed the same phenomena and recommended close attention to the regularity of micturition in patients treated with ergot and, should retention occur, the use of the catheter. (Evetzky).

Absorption and Elimination.—The active constituents of ergot are rapidly absorbed into the blood and are eliminated principally by the kidneys, increasing the urinary flow. It is well established that ergot does not pass into the milk. Evetzky discovered a substance resembling ergot in a womb discharge of a woman treated with ergot for a uterine fibroid tumor.

Muscle.—In therapeutic doses the principal action of ergot is on unstriped muscle fiber. It causes especially the contraction of the blood vessels and of the uterus. Some experiments made by the writer indicated that the gastrocnemins muscle of the frog contracted somewhat more forcibly under the influence of ergot.

EXPERIMENTAL.

The action of ergot upon the uterus is quite fully described in the text books on materia medica, but any literature bearing upon direct experimental evidence of this action, the writer was unable to discover. The experimental work was, therefore, confined almost entirely to a study of this drug upon the uterus of pregnant cats.

I am indebted to Dr. P. A. Fish for the data of two experiments upon pregnant cats, which he carried out in the Spring of 1904. On April 16, he injected hypodermically 1 cc of aseptic ergot (Parke Davis) at intervals of about one hour until five doses had been administered. On the following day April 17, it was found that the cat had given birth to three living kittens which were well enough developed to nurse from the mother. The mother appeared bright and did well afterwards.

Cat number 2 was experimented upon the same day ; but in

this instance the fluid extract of ergot (Parke Davis) was used. One dram of the fluid extract diluted with two drams of water, was administered through a rubber tube, directly into the stomach. Five doses were administered in all at about one hour intervals. On the following day (April 17) it was found that two dead but quite fully developed kittens had been born. On the morning of April 18, another dead kitten was found and the mother seemed to be in considerable distress. At 2 P. M. she was found dead. The postmortem showed two more kittens in the uterus. One with head presenting in the vagina and badly squeezed out of its natural shape. The uterus was much congested and appeared to be almost gangrenous, with considerable bloody exudate in the abdominal cavity.

The remaining experiments were carried on under the direction of Dr. Fish, the special object being to note the oxytocic properties of the drug and incidentally the after effects upon the mother and fetus. In the majority of cases the fluid extract of ergot (Parke Davis) was used; the dose being one dram diluted with two drams of water introduced directly into the stomach through a rubber tube.

Cat No. 3. On March 21, 1905, four doses of the fluid extract were administered as above described at intervals of two hours. On the following day no signs of abortion were observed although the cat seemed slightly indisposed. On March 23, five doses of the drug were given at similar intervals, but no symptoms were observed on the following day. On April 8, the experiment was repeated but the ergot was given at intervals of one hour instead of two. On the following day at 10 A. M. the cat seemed uneasy, looking around at the flank and appearing as if to make preparation for the act of parturition. At 10:45 she gave birth to four kittens, two of them dead. At 2 P. M. she gave birth to another live kitten. The following day all of the kittens were dead except one and this lived only twenty-four hours longer. The kittens seemed quite well developed although small. They were not seen to suck nor did mammitis develop in the mother.

Cat No. 4. On April 22, one dram doses of the fluid-extract were administered every half hour up to five doses. No symptoms

were observed on the following day except slight muscular tremblings. On April 25, four doses were given at half hour intervals. Shortly after the fourth dose she gave birth to a kitten (10:30 A. M.). At 2 P. M. another kitten was born. These kittens were smaller and possessed less hair than those of No. 3. The cat was more indisposed and did not recover so rapidly as No. 3.

Cat No. 5. The experiment was carried out as on No. 4. Emesis occurred after the third dose. Dosage was begun at 4 P. M. May 3 and at 9 A. M. the following morning she gave birth to a kitten quite immature and less than half grown. It measured only 5.6 centimeters in its fetal membranes. No other kittens were observed. On May 9 the cat was killed and a postmortem held. The uterus showed that four kittens had been present and it was assumed that the mother ate up the remaining immature kittens as she was not constantly observed during the whole of the experiment. The mother's health had been excellent up to the time ofthe postmortem.

Cat No. 6. On May 19 four doses of ergot were administered at half hour intervals. There were no results on the following day. Similar doses were administered May 22, with emesis after the third dose. No abortion or other symptoms were observed. The cat was killed and four kittens near term were found in the uterus.

Three other cats were experimented upon, but the postmortems showed they were not pregnant.

SUMMARY AND CONCLUSIONS.

Of the six pregnant cats experimented upon, five gave birth to their young within a reasonable time after the administration of the ergot. Some of the kittens were probably near term, because of this it may be suggested that normal labor may have occurred independently of the ergot. In the absence of any data relating to the time of impregnation absolute proof is impossible; but the fact that cats 1 to 5 inclusive gave birth to their kittens within twenty-four hours after the last dose of ergot, renders it highly probable that the act of parturition was not a coincidence correlated with normal labor, but was due to the action of the ergot.

In cats 1 and 2 the treatment was simultaneous (except for the form of the preparation of the drug); the act of parturition was also simultaneous. This fact, it seems to us, is deserving of more weight than that the kittens were near term.

Cat No. 3 required three sets of experiments at intervals of a few days before parturition effects were produced. The kittens although apparently quite well developed were small. Two of them were born dead. The remaining three were unable to nurse and soon died ; and the conclusion was reached that they were born prematurely.

On cat No. 4, two sets of experiments were tried within an interval of three days. Shortly after the last dose the act of parturition set in. The kittens were even more immature than those from cat No. 3, and their birth is quite reasonably attributed to the action of the ergot.

On cat No. 5, the ergot unquestionably produced abortion, as the kitten was not more than half its term and measured only 5.6 centimeters in length. This experiment emphasized the necessity of close observation because of the tendency of the mother to eat the immature young. If the act of parturition is not observed and if no fetus is found (because of its having been eaten), the conclusion would be reached that the drug had exerted no action.

Two sets of experiments, within an interval of three days, were performed upon cat No. 6 without result. It is possible that more of the drug was needed in this case as in cat No. 3, or that the cat was less susceptible than the others.

The effect of the ergot upon the mothers was apparently not harmful except in cat No. 2 where there was a fatal termination and in cat No. 4 where there was some indisposition for a time, but ultimate recovery ensued.

In some cases a few of the fetuses were born dead, and others died soon after birth, while a few survived. The former conditions might be expected if the birth was premature.

From these experiments the conclusion seems reasonable that ergot has the power of stimulating the gravid uterus to the extent of emptying it of its contents, in the cat.

Some difference in susceptibility was noted. Cats Nos. 1 and 2 required only five doses. Cat No. 3 required fourteen doses in three series of experiments and Nos. 4 and 5 nine doses in two series of experiments.

The doses should be rather large and administered with due frequency in order to produce abortion.

THE STATUS OF THERAPEUTICS.

PIERRE A. FISH.

ITHACA, N. Y.

The veterinarian who has merely a financial interest in his patients, is unworthy of the name. The highest aim of the true practitioner is to cure disease and alleviate suffering. In addition the thinking practitioner seeks to know how and why the results are effected.

Therapeutics is not an exact science ; it is slowly struggling toward that goal. Ignorance of causes retards therapeutic efficiency. Therapeutics has kept pace with the wonderful progress of pathology in the last few decades, and new treatments have been worked out to correspond with the increased knowledge of the origins of morbid effects. Most of the glory for these discoveries has gone to pathology but, richly as she deserves it, therapeutics should not be forgotten.

Therapeutics is ancient ; she was born in mysticism, has developed into science, and is the keystone of practice. She has brought surgery out of the dark ages by bestowing upon her the blessings of anesthesia and asepsis. The brilliant and radical operations that may now be performed with comparative safety, were undreamed of some years ago. The result has beeu that, in the eyes of some, such a glamour has encompassed surgery that therapeutics has become hidden in obscurity. In certain cases, surgery may with a few strokes of the knife, as in the removal of a benign tumor, dissect out the disease and cast it away. Just as brilliant an operation, to my mind, is, with purely therapeutic measures, to convert a patient rolling in the agonies of colic into a quiet, peaceful, normal, and contented frame of mind with little prospect of recurrence of the trouble under proper conditions of care.

But there are major operations which may be complicated with infection, where recovery is slow and prolonged, or where death

occurs. Similarly in a medical case the practitioner may be groping in the dark, or the drugs are not potent enough to set up the proper reaction in the affected tissues. Yet, equal in glory and comparable to the most successful major operation, it seems to me, is the restoration to a normal condition of a lung or a portion of it, which has become consolidated and therefore practically functionless for respiratory purposes. The regulation of the heart and circulation, breathing, peristalsis, the increase or decrease of the various secretions of the body by therapeutic measures, is as wonderful to me as any surgical operation that has ever been devised. Surgery, however, has the advantage of being able to cut her way to the foe and can *see* more or less clearly its nature and the extent involved. Medicine cannot do this; her foe is concealed and must therefore be fought in the dark, with the result that very often the various stages in the fight cannot be seen clearly at a given time. It is natural that one should expect more from him that fights a visible enemy than from one who attacks a hidden foe; but in the event of victory for the latter the glory should be greater.

New Remedies. The number of new remedies discovered each year is surprising. But a small fraction of them come into practical use and that often for only a short time. The great majority have no superior merit over the old ones and are no more heard of.

It is safe to say that many of the old and experienced remedies will never be superseded, and that there is still much to be learned of their virtues, there can be no doubt.

The scriptural saying, "Prove all things and hold fast to that which is good" applies with more or less force here. Conservatism is the safer procedure. Undue eagerness is to be deprecated. Wait until some of the merits of the new drug have been demonstrated; but having once decided to try it, give it a faithful, fair, impartial and sufficiently prolonged test to determine conclusively in your own mind its value or its uselessness.

Secret Remedies. This term is used advisedly as against *patent medicines*. In patenting a remedy, the formula must be given to the patent office and this office may give out the formula to those who may desire it upon the payment of a fee. This, of course is

just what the manufacturers do not wish. Secrecy is their prime object, and must be maintained so they have very little use for patents. In secrecy exists the harm. The practitioner has no guarantee that the concoction contains the proper ingredients indicated for the disorder ; they may indeed aggravate it. There is no certainty that a new supply of the secret remedy will be identical with that previously obtained. Secrecy encourages fraud. It is difficult to conceive that the manufacturers of such products are animated by any noble ideas of humanitarianism. The principal idea seems to be to sell at a maximum price certain ingredients which have been assembled at a minimum of cost.

The practitioner who enters the gateway of secret remedies may well leave hope behind. His dependence is upon luck and whatever amount of scientific discrimination and therapeutic discernment he may have possessed is speedily deteriorated ; because he *hopes* the disorder may yield to an unkuown preparation. Blind dependence replaces therapeutic independence. Secret remedies are dangerous, unethical and demoralizing to the practitioner.

Another class of preparations without the element of secrecy or only partially so, in which the ingredients are named but the proportions witheld, may be grouped among the *commercial* preparations. Such drugs may at times be of value but the therapeutist may, to some extent, be hampered by the incompleteness of his knowledge.

The highest aim of the practitioner is to preserve his patient from death. If from his own knowledge, or from the experience of others, this can be accomplished only by the use of a secret remedy, what then, is his duty? Any means to preserve life is the humane view. Such a contingency, however, is so exceedingly remote that very few practitioners are called upon to dicide an issue of that character.

Active Principle Medication. The tendency in recent years has been to use purer, not cheaper, drugs ; to remove the inert material and get down to the basic principles of the plant. The use of the alkaloids, glucosides, resins, etc. will undoubtely increase still more in the future as their convenience and efficacy are experienced. The galenical preparations are not always standardized, and many

of them contain more than one active principles. Depending upon the relative proportion of these principles, the combination may have a very satisfactory effect in certain cases. Similar effects, however, may be reached with the isolated principles if properly combined.

Isolated principles have the advantage of greater precision in their effects in that they are unembarrassed by the side action of subsidiary principles or by the presence of any restraining or inert material.

They enable the practitioner to control with greater ease the physiologic or pathologic conditions of the body. As now prepared they are convenient to carry, pleasant to take and easy to administer.

In the treatment of the larger domestic animals, unfortunately, they are not so readily available for continued treatment, except by the hypodermic method; and it is scarcely practicable to entrust this to the layman no matter how well intentioned he may be. It is by no means impossible that the future may solve this difficulty. In the case of the smaller animals, alkaloidal treatment is extremely convenient and efficacious, and is coming more and more into use.

Therapeutics is as old as medicine itself. Its value has been overshadowed at times by brilliant discoveries in collateral fields. It has emerged from temporary obscurity with its luster undimmed. It is dependent upon other sciences but directs them. It is the ultimate end of medicine, surgery and pathology. Its status is as old as the hills, yet it is as recent as the light of today. The study and investigation of therapeutic effects and affinities is infinite. The overwhelmingness of such research is well alluded to by Harley in his perface to 'The Old Vegetable Neurotics', from which I quote: "Our first impressions on entering the wilderness of thera peutical inquiry must indeed be discouraging, and the prospect of reducing anything to order, at first sight, hopeless. A lifetime will seem too short to effect any change, and we shall be inclined to turn back. But let us shut out the desert and the jungle from our view, and turn to the nearest object. Let us clear away the suffocating undergrowth from about it, denude it of the tangled climbers

that conceal its trunk, and the moss which covers its branches. Let us lop off the parasites that deform it, and the foreign branches, it may be, which some previous hand has engrafted, and, thus isolated and reduced to its natural simplicity, let us choose it as the special object of our study and care. Life may be long enough to know this single individual ; and if we each one effect so much, what is now an uncultivated wild with scarcely one well-ordered patch to rest the eyes upon, will soon show signs of culture ; and with continued labor become in future generations a fair garden—a health resort—where, with simple directions, we may send our patients to cull the good gifts which a Beneficent Hand has planted and purposed for the relief of the 'thousand ills that flesh is heir to'."

THE STRUCTURE AND FUNCTION OF THE DIGESTIVE TRACT OF THE CHICKEN.

FREDERICK H. MC NAIR.

McDaniel of Ohio University made quite an exhaustive study of the histological structure of the chicken's digestive tract and observed as follows :—

That the crop is not only a reservoir for food but also softens it.

That the alimentary tract, from esophagus down, consists of three coats, fibrous, muscular and mucous, the muscular coat being in 3 layers like that of mammals.

The proventriculus or fore stomach is about 4 cm. long in the adult chicken and is separated from the gizzard by a sphincter muscle. It appears to be simply an enlargement of the esophagus but is not so strongly marked on its inner aspect by longitudinal folds, hence is not so expansible and the mucosa contains a different type of glands which have large openings and extrude the gastric juice.

The gizzard, contrary to older writers on the subject, possesses not only a muscular (triturating) function, but also probably secretes a digestive fluid. On the inner face of its mucosa is a horny layer which is probably an aid to the grinding of food.

The pancreas is about 3 inches long and narrow and lies within a loop of the duodenum being closely attached to both sides and emptying into the duodenum by one duct at each end.

Throughout the intestines lymph nodules were found in the mucosa, being especially numerous in the ceca which seems to indicate that they are organs of absorption.

Mitchell regards the ceca as a heritage from reptilian ancestors and if large to retain digestive functions.

My own study was confined to the proventriculus, gizzard and ceca. The statements of McDaniels as to the histological structure of these parts were verified. The three muscular coats throughout; the secretory cells in both proventriculus and gizzard ; the horny

layer on the inner face of the gizzard mucosa and the lymph nodules in the walls of the ceca were all easily distinguished in microscopic sections.

The size of the proventricular glands is astonishing, the elevated openings on the mucosa being as large as pin heads.

A long search was made to find if the gastric cells corresponded to the principal (pepsin) cells of mammals. Only one class of cell could be discovered which is, according to Oppel, neither principal nor parietal but a primitive type with complex function. This complexity of function I sought to verify by numerous laboratory tests with both artificial and fresh gastric juice.

The artificial extract was made by dissecting the proventricular mucosa away from the muscular portions then grinding them rather finely in a meat chopper and bottling them with sufficient glycerin to cover. In all cases the gastric secretion was found to be quite strongly acid in reaction.

After standing in a cool place for 2 months the glycerin extracts were fiiltered through paper, some distilled water being also passed through the paper to insure the passage of all the extract. The resulting filtrate was an amber colored, viscid liquid. About equal quantities of chicken and turkey extract were prepared in this way, care being taken to keep them separate, and used in the following tests :—About 5 cc of each extract were placed in test tubes containing blood albumin, boiled fibrin, starch paste, raw meat, cooked meat and milk respectively. To the tubes containing starch paste and milk a little 1% sodium carbonate was added to render slightly alkaline ; to the other tubes was added 0.2% HCl to render more acid. All the tubes were plugged with cotton and incubated for 18–24 hours at 40° C. Tested the albumin, fibrin and meat tubes for syntonin, albumose and peptone. For syntonin by adding litmus solution to color then neutralizing with a dilute alkali. For albumose by ammonium sulphate and biuret tests. For peptone by precipitating the albumose with neutral ammonium sulphate filtering and applying the biuret test to the filtrate. In every case only albumose was found which was quite pronounced from the cooked meat. Check tubes were always used containing the various sub-

stances to be digested and 0.2 % HCl, also tubes of the extract alone acidulated with HCl. In two cases only a slight albumose reaction was obtained from the latter, probably due to some particles of muscle present.

Tested the starch tubes for reducing sugars by Feblings and Boettgers tests. Slight reduction was obtained a number of times and pronounced reduction twice. The value of these sugar tests was lessened because it was found that glycerin acidulated with 0.2% HCl, allowed to stand a day or two then rendered alkaline with 1% sodium carbonate, starch paste added and the tubes incubated as before as a check, a sugar reaction was obtained.

The test for a milk curdling enzyme was not satisfactory although a slight curdling resulted in one or two cases.

To substantiate the above results some fresh chicken proventriculi and gizzards were obtained. The proventriculi were opened and all food particles gently removed and by a squeezing and scraping process the juice was collected and put in a little chloroform water to preserve it. The juice varied from a cream to a straw color, being darker and mucoid on the free surface. This extract was added to blood albumin in test tubes, incubated and tested as before. A good albumose reaction was obtained, the reaction being stronger when a litte 0.2% HCl had been previously added to the mixture although the juice itself was quite strongly acid in reaction. Check tubes containing the gastric juice and 0.2% HCl gave no albumose or peptone reaction. Other portions of the fresh gastric juice were rendered alkaline with 1% sodium carbonate, starch paste added and incubated as before. Applying the sugar tests slight reactions were obtained. Check tubes containing starch paste, sodium carbonate and chloroform water did not respond to the sugar tests.

Strips of the gizzard mucosa, which had been washed free of food material, were placed in test tubes containing a little distilled water, acidulated with 0.2% HCl, dried blood albumin and 1 cc of chloroform water to preserve it ; incubated for 22 hours at 40° C, then tested for albumose and peptone. A strong albumose and a slight peptone reaction were obtained. The experiment was repeated with the same results but checks containing the same sub-

stances, minus the albumin, gave no reaction. Washed strips of the gizzard mucosa were now put in test tubes containing chloroform water, sodium carbonate to render alkaline, and starch paste and incubated over night. A strong sugar reaction was obtained with Fehling's and Boettger's tests. The experiment was repeated, the mucosa first having been throughly washed in running water, at the same time rubbing with the fingers to remove all traces of food material and any proventricular secretion that may have lodged there. The reducing sugar reactions obtained were just as pronounced as before. Checks containing the other constituents with starch-paste left out, also checks with the mucosa only left out, gave no sugar reactions.

To determine the value of a ration of molasses for fattening purposes two brown leghorn hens were obtained and kept in an indoor pen 5x7 ft. and fed as much yellow corn meal mixed with molasses and water to make a thick mush, as they would eat up clean. The amount of meal was at first 4 oz. and 1 oz. of molasses per day for the two ; later the molasses was increased to 2 oz. From December 13 to January 11 they were fed on corn meal mush alone and then hen No. 1 weighed 3½ pounds, an increase of ½ a pound ; hen No. 2 weighed 3 pounds, also an increase of ½ pound.
January 11 began feeding the molasses in ration. February 21 hen No. 1 weighed 4½ pounds, an increase of 1 pound, and hen No. 2 weighed 3½ pounds an increase of ½ pound. Throughout the test the hens were kept supplied with water and a small amount of grit: After the first day or two the ration was eaten with evident relish.

During the past winter arrangements were made with the Poultry department of the University and a comparative test carried on under the supervision of Professor Jas. Rice. Two pens, containing 9 full grown chickens each, were used, and the experimental feeding continued for 21 days. The rations were :

For pen No. 1—

Corn meal 8 oz.; middlings 2 oz.; boiled potatoes 6 oz.; meat scraps ¼ oz.; oil meal ¼ oz. per day.

For pen No. 2—

The same ration with the addition of ½ oz. of common molasses

per head each day for one week which, for the two following weeks, was increased to one ounce per head per day.

At the end of 7 days the collective gain for the 9 chickens for the week was	for pen No. 1, 2.4 pounds, for pen No. 2, 3.9 pounds.
At the end of 14 days the collective gain for the 9 chickens over the first week was	for pen No. 1, 6.5 pounds, for pen No. 2, 7.3 pounds.
At the end of 21 days the collective gain for the 9 chickens over the second week was	for pen No. 1, 1.9 pounds, for pen No. 2, 3.7 pounds.

This makes a total gain in favor of the pen of molasses fed fowls of 4.1 pounds or an average gain per fowl of 0.45 pound. At the price paid for the molasses, 40 cents a gallon, there was not much profit on such a ration. By purchasing a cheap grade of molasses in bulk, feeding at least an ounce of it per head each day, omitting from the ration the oil meal and part of the potatoes, a decided gain in profit should be made on molasses fattened fowls. The ration was eagerly eaten and with little waste.

March 20, hen No. 1 was operated on, the intestine being separated from the ceca and an artificial anus made. This was done to determine whether or not the ceca bear any relation to absorption.

DESCRIPTIVE HEN NO. 1.

DATE	WEIGHT	
March 20.	$4\frac{1}{2}$ lbs.	Hen fat and in excellent health and having a good appetite. Anesthetized with ether ; pulled out feathers for a space of three inches in diameter immediately anterior to anus ; disinfected area and Dr. Fish operated as follows ; Made a longitudinal incision $1\frac{1}{2}$ inches long anterior to anus, and into peritoneal cavity, gently pulled out as much of the intestine as

DATE	WEIGHT	
		necessary and, after ligating, amputated it at about the level of the tips of the ceca and with catgut stitched the cut end of the intestine to the external edges of body incision, thus making an artificial anus and leaving the ceca, cloaca, and 5 or 6 inches of the intestine detached from the digestive tract.
		The egg sac was accidentally cut into and some egg yolk discharged. The wound around the artificial anus was sutured. About 15 minutes were required to complete the operation. Hen soon recovered from the effects of the ether and discharged from the true anus a small amount of bloody feces.
March 21.		Appears bright ; passed feces several times during the day. No food given. Water.
March 22.		Condition same ; liquid feces passed apparently from true anus as they were well mixed with urine. Forced a little milk down throat.
March 23.		Condition unchanged. Gave 2 oz. of milk and a little corn meal forcibly.
March 24.		Still some liquid feces, origin not determined. Passed a probe several inches into artificial anus, and injected a little olive oil to keep the parts soft. Hen began eating meal and molasses again.
March 25.		Some feces passed from artificial anus. Parts hot and inflamed. Appetite good. Gave some cotton seed oil per mouth.
March 26.		Condition same. Appetite still good.
March 27.		Bright and eating. Gave oil enema by artificial anus ; dark feces expelled.
March 28.	4 lbs.	Still bright. Dark feces passed.
March 29.		Losing condition ; rather dull. Stitches

DATE	WEIGHT	
		above artificial anus ripped out by swelling of parts. Appetite poor.
March 30.	$3\frac{1}{2}$ lbs.	Dull and drooping. Comb pale; feces black; urine green; appetite poor.
March 31.	$3\frac{1}{2}$ lbs.	Very dumpish. Forced a little corn mush down throat and gave $\frac{1}{2}$ gr. calcium sulphide. Gave enema of glycerin and water equal parts.
April 1.	$3\frac{1}{2}$ lbs.	Very dumpish; ate nothing; feces black; urine yellow; gave enema of water.
April 2.		No treatment; ate nothing.
April 3.	$3\frac{1}{2}$ lbs.	Acts brighter; ate a little mush; gave $\frac{1}{2}$ gr. calcium sulphide; enema of glycerin and water, no feces resulted; urine dark and thick.

Condition remained about the same, no appetite and she gradually grew weaker till death occurred April 14; weight 3 pounds.

POST MORTEM NOTES.

Crop contained fluid mass of oil and meal given a week before. Odor of calcium sulphide detected.

At the field of operation a scab had formed over the artificial anus so that there was no outlet for feces. When the scab was removed a small opening was found to be present. Absence of a sphincter ani at this point made voluntary defecation difficult. Intestine, for 10–12 inches forward from artificial anus, much enlarged and contained a considerable quantity of dark colored, soft feces. Strong odor of calcium sulphide present which blackened the probe used in exploration. The ceca and remnant of rectum apparently much atrophied and entirely empty. Liver dark and gall bladder distended. Heart collapsed and hen apparently anemic. The wound was completely healed.

In collecting the proventriculi from the local markets I was impressed with the distension of the ceca, especially in the turkeys; some of the latter being $1\frac{1}{2}$ inch in diameter and fillled with hard, dark feces. Considering this fact, and the profound ill effects pro-

duced in the hen by the separation of the ceca from the digestive tract, it would seem that the ceca are vitally concerned in absorption. This is further confirmed by the presence in the cecal walls of lymph nodules as noted by McDaniels.

SUMMARY.

1. Histologically the digestive tract of the chicken resembles somewhat that of mammals but the type is primitive. In the proventriculus there is only one type of cell which is neither principal (pepsin) nor parietal (acid) but possesses a complex function, secreting pepsin, acid and a starch digesting enzyme. Thus the evolutionary chain is strengthened.

2. The gizzard in spite of former statements to the contrary, apparently has more than a mechanical function as washed portions of the mucosa digested dried albumin and converted starch into sugar. Moreover microscopic sections revealed cells quite similar in appearance to the proventricular cells.

3. The ceca are evidently concerned in absorption, or at least exert considerable influence upon bodily health as separation of them from the digestive tract caused a loss of weight and condition.

4. Molasses is a valuable addition to a fattening ration for chickens and probably for all poultry.

THE EFFECT OF SULPHUROUS ACID UPON THE URINARY CONSTITUENTS.

PIERRE A. FISH.

As the largest share of the elimination of absorbed substances undoubtedly falls upon the kidneys, the examination of the urine will aid materially in affording a comprehensive view of the metabolism of the tissues.

Two young men were utilized in this experiment, each receiving 15 minims (a fair minimum medicinal dose) of sulphurous acid, three times daily, shortly after each meal. The total amount of urine for the 24 hours was collected and a sample of it analyzed. This was continued for seven days—as long as the sulphurous acid was taken. During the following week—when no acid was taken, the urine was collected as before and samples analyzed for comparison.

Neither of the subjects appeared to suffer any ill effects from the use of the agent. There was no change in their duties or manner of living during the period of observation and their appearance was normal so far as could be detected.

The following table gives the average amount of the urinary constituents and the average quantity of the urine for each week while the experiment was carried on.

Subject No. 1	Average of Urinary Constituents during the use of H_2SO_3	Average of Urinary Constituents when no H_2SO_3 was taken
Quantity of Urine	875 cc	757 cc
Specific gravity	1.0268	1.0265
Solids per liter	62.57 grams	61.91 grams
Chlorides per liter	16.94 "	16.75 "
Sulphates per liter	2.03 "	2.40 "
Phosphates per liter	2.69 "	2.80 "
Urea per liter	32.40 "	32.20 "

Subject No. 2

Quantity of Urine	1067 cc	1087 cc
Specific gravity	1.0268	1.0255
Solids per liter	67.09 grams	61.43 grams
Chlorides per liter	17.27 "	16.95 "
Sulphates per liter	2.93 "	2.71 "
Phosphates per liter	1.89 "	2.11 "
Urea per liter	35.00 "	33.40 "

A comparison of the tables shows that during the sulphurous acid period both subjects gave urine with a higher specific gravity indicating the presence of a greater quantity of solids. The chlorides and urea were also increased, while the phosphates were decreased. Up to this point both subjects agree in their results. Points of disagreement are first: in the amount of urine, No. 1 showing some diuresis while No. 2 did not. Second in the sulphate constituent, No. 1 showing a greater quantity during the normal period, while No. 2 showed the greater quantity during the sulphurous acid period.

On the whole, tissue metabolism was evidently stimulated as shown by the increased amount of solids,—especially urea and chlorides. No unfavorable effects were noted from the doses given.

Compliments of
PIERRE A. FISH

ABSTRACTS

OF

WORK DONE IN THE LABORATORY

OF

VETERINARY PHYSIOLOGY AND PHARMACOLOGY

UNDER THE DIRECTION OF P. A. FISH

NO. 4

NEW YORK STATE VETERINARY COLLEGE
CORNELL UNIVERSITY
ITHACA, N. Y.
1907

TABLE OF CONTENTS.

SODIUM BENZOATE AND THE DIGESTIVE ENZYMES.

PIERRE A. FISH.

Aside from its therapeutic uses, sodium benzoate deserves interest from the fact that it has been used to a considerable extent as a food preservative. Whether it is favorable or detrimental to digestion is, therefore, a matter of twofold significance; because as a food preservative conditions of health are involved, while from the therapeutic standpoint diseased conditions are concerned.

The results of the following experiments may, therefore, be of some use from both standpoints. Varying amounts of the drug have been used and that there should be, within certain limits, correlative variations in the results might naturally be expected.

Salivary Digestion. The reagents were first tested in order to determine their purity. The sodium benzoate was found to be neutral in reaction and had no reducing influence upon Fehling's Solution. The starch was found to be free from any reducing sugar. Fehling's method, as described by Leach, was employed in determining the amount of reducing sugar present in the different experiments. The Fehling's was prepared so that each 10 cc. would be completely reduced by 0.05 gram of dextrose.

Experiment 1. In this experiment 2½ grams of starch were boiled in 60 cc. of water. To this was added 1 gram of sodium benzoate dissolved in 30 cc. of water. This mixture was allowed to stand 17 hours and then 30 cc. of filtered saliva were added and digestion allowed to continue for one hour at a temperature of 38° to 40° C.

Qualitative tests showed the presence of sugar within 25 minutes.

Experiment 1-a. This was similar to No. 1 in every way except that no sodium benzoate was present. Sugar was also found in this flask within 25 minutes.

Quantitative tests of the contents of the two flasks showed that 5 cc. from flask No. 1 were sufficient to reduce the Fehling's or that each 5 cc. of the benzoated flask contained 0.05 gram of reducing sugar. In No. 1-a only 4.3 cc. of the solution were required to reduce the Fehling's so that the evidence was in favor of the latter or normal flask.

Experiment 2. This was similar to No. 1, except that the saliva was kept in the ice chest for 17 hours and then at room temperature for 7 hours before digestion began. Sugar was found in this flask within 10 minutes.

Experiment 2-a. Similar to No. 2, except that no sodium benzoate was present. Sugar was also detected in this flask within 10 minutes after the beginning of digestion.

At the end of the hour, quantitative tests showed that only 4.8 cc. of the solution from flask 2 were required to reduce the Fehling's Solution; while in the normal flask No. 2-a only 3.7 cc. were required.

Experiment 3. In this experiment the same amount of sodium benzoate was used. Its solution was added to the saliva and the mixture kept in the ice chest for 17 hours, and later 7 hours at room temperature, before mixing with the starch and beginning digestion. Sugar was found to be present within 5 minutes.

Experiment 3-a. Similar to No. 3, except that no sodium benzoate was present. Sugar was also found in this flask within 5 minutes.

Quantitative tests showed that 5.1 cc. of the benzoated mixture were required to reduce the Fehling's Solution; while in the normal mixture (No. 3-a) only 3.9 cc. were required.

The following summary of the experiments is useful for comparison:

Sodium Benzoate.		Normal.	
No. 1.	5 cc.	No. 1-a.	4.3 cc.
No. 2.	4.8 cc.	No. 2-a.	3.7 cc.
No. 3.	5.1 cc.	No. 3-a.	3.9 cc.
Average	4.96 cc.	Average	3.96 cc.

The evidence in these experiments is uniformly in favor of the normal flasks.

Experiment 4. In this experiment the saliva was diluted one-half with distilled water. Digestion was allowed to continue 3½ hours at a temperature of 38° to 40° C. The starch mixture and the sodium benzoate solution were mixed shortly before adding the saliva.

Flask No. 1 (Normal). 2½ grams starch + 60 cc. water + 30 cc. diluted saliva.
Flask No. 2. 2½ grams starch + 60 cc. water + 1 gram sodium benzoate in 30 cc. water + 30 cc. diluted saliva.
Flask No. 3 (Normal). 1 gram starch + 50 cc. water + 25 cc. water + 25 cc. diluted saliva.
Flask No. 4. 1 gram starch + 50 cc. water + 1 gram sodium benzoate in 25 cc. water + 25 cc. diluted saliva.
Flask No. 5. 1 gram starch + 50 cc. water + 0.5 gram sodium benzoate in 25 cc. water + 25 cc. diluted saliva.

The proportion of sodium benzoate in the benzoated flasks was as follows: No. 2, 1 to 120 or $\frac{5}{6}$%; No. 4, 1 to 100 or 1%; No. 5, 1 to 200 or 0.5%. The flasks were submitted to the same experimental conditions and when digestion was discontinued the quantitative tests showed the following results:

No. 1 (Normal). Only 2.5 cc. of the mixture were required to reduce the Fehling's solution.

No. 2. 4.5 cc. of the mixture reduced Fehling's.

No. 3 (Normal). 7.2 cc. reduced Fehling's.

No. 4. 7.2 cc. reduced Fehling's.

No. 5. 7.8 cc. reduced Fehling's.

In all of the flasks, there was present the same amount of saliva, but there was a variation in the amount of starch; two of the flasks having 2½ times as much as the remaining three. It seems reasonable, therefore, to infer that a greater amount of sugar had been formed in those flasks where there was the greatest amount of starch. As regards flasks 1 and 2, the evidence is decidedly in favor of No. 1; there being more sugar in the normal than in the benzoated flask. In the three flasks containing the smaller proportion of starch, the results were much alike and would lead to the inference that the presence of the benzoate

in the flasks 4 and 5 had but little if any influence upon the salivary digestion. The evidence as a whole, however, seems to be more favorable to the normal than to the benzoated flasks.

GASTRIC DIGESTION. *Pepsin.* The experimental work with the enzyme pepsin included such food stuffs as egg albumin, raw meat and fibrin.

Experiment 5. An artificial digestive fluid was prepared by dissolving 0.0535 gram of scale pepsin in 1000 cc. of 0.2% hydrochloric acid. Portions of this stock solution were used in the experiments on albumin. The albumin was obtained from hard boiled eggs. The whites of the eggs being forced through a finely meshed sieve in order to get them in a finely divided state.

Flask No. 1. Control. 10 grams of egg albumin + 30 cc. of the pepsin solution.

Flask No. 2. 10 grams of egg albumin + 30 cc. pepsin solution + 1 gram sodium benzoate in 30 cc. of water.

Flask No. 3. Second control. 10 grams of egg albumin + 50 cc. of the pepsin solution.

Flask No. 4. 10 grams of egg albumin + 50 cc. pepsin solution + 1 gram sodium benzoate in 50 cc. of water.

Flask No. 5. 10 grams of egg albumin + 50 cc. pepsin solution + 0.5 gram sodium benzoate in 50 cc. of water.

Flask No. 6. 10 grams of egg albumin + 50 cc. pepsin solution + 0.25 gram sodium benzoate in 50 cc. of water.

Flask No. 7. 10 grams of egg albumin + 50 cc. pepsin solution + 0.125 gram sodium benzoate in 50 cc. of water.

Flask No. 8. 10 grams of egg albumin + 50 cc. pepsin solution + 0.0625 gram sodium benzoate in 50 cc. of water.

On mixing the ingredients, the contents of flasks 2 and 4 became turbid and a precipitate formed; the other flasks remained comparatively clear. The formation of the precipitate was probably due to the action of the hydrochloric acid upon the sodium benzoate, causing the production of benzoic acid, which is not readily soluble in water. All of the flasks were allowed to digest for 22 hours at a temperature of 38° to 40° C. At the end of digestion, each of the flasks was tested for the intermediate and end products of digestion. Peptones were found in all of the flasks but numbers 2 and 4. Intermediate products were also absent in these two flasks. After the filtering of the contents of the flasks, the undissolved residues were dried to constant weight and then weighed. The following table shows the results:

		Percentage of Albumin Dissolved.	Percentage of Undigested Residue.
Flask No. 1.	Control.	91.87%	8.13%
Flask No. 2.	$1\frac{2}{3}$% Benzoate.	83.99%	16.01%
Flask No. 3.	2d Control.	98.12%	1.88%
Flask No. 4.	1% Benzoate.	84.50%	15.50%
Flask No. 5.	0.5% Benzoate.	91.37%	8.63%
Flask No. 6.	0.25% Benzoate.	98.20%	1.80%
Flask No. 7.	0.125% Benzoate.	98.27%	1.73%
Flask No. 8.	0.0625% Benzoate.	98.63%	1.37%

In flask No. 2 which contained sodium benzoate to the extent of $1\frac{2}{3}$% and No. 4 which contained 1% no digestion occurred as shown by the absence of peptones. Although the table shows that approximately 84% of solid material had disappeared in each case, it must be remembered that the original 10 grams of egg albumin contained a large percentage of water and that when dried to constant weight and with no digestive action, there would be a large decrease in weight on account of the loss of water. In flask No. 5, which contained 0.5% of benzoate, peptones were present but the relatively large amount of undigested residue would indicate that digestion had been retarded. In flask No. 3 (control) and in numbers 6, 7 and 8, containing 0.25% or less of benzoate, the results were very similar to each other and would indicate that 0.25% or less of the benzoate had no interference with the digestion. Incidentally the antiseptic effects of sodium benzoate were noted in this experiment. The filtrates from the flasks were retained five weeks. At the end of this period the controls Nos. 1 and 3 showed a profuse growth of mould while the benzoated flasks remained clear.

Experiment 6. This experiment was the same as No. 5 except that raw beef finely divided was substituted for the egg albumin.

Flask No. 1. Control. 2 grams raw meat + 30 cc. water + 30 cc. pepsin solution.
Flask No. 2. 2 grams meat + 30 cc. pepsin solution + 1 gram sodium benzoate in 30 cc. water.
Flask No. 3. 2d control. 2 grams meat + 50 cc. pepsin solution + 50 cc. water.
Flask No. 4. 2 grams meat + 50 cc. pepsin solution + 1 gram sodium benzoate in 50 cc. water.
Flask No. 5. 2 grams meat + 50 cc. pepsin solution + 0.5 gram sodium benzoate in 50 cc. water.

Flask No. 6. 2 grams meat + 50 cc. pepsin solution + 0.25 gram sodium benzoate in 50 cc. water.

Flask No. 7. 2 grams meat + 50 cc. pepsin solution + 0.125 gram sodium benzoate in 50 cc. water.

Flask No. 8. 2 grams meat + 50 cc. pepsin solution + 0.0625 gram of sodium benzoate in 50 cc. of water.

Flasks Nos. 2 and 4 showed a precipitate of benzoic acid as did the similar flasks in the preceding experiment. Digestion was allowed to go on for 15 hours at a temperature of 38° to 40° C. No peptones nor intermediate products were found in the contents of flasks 2 and 4, showing that no digestion had occurred here. In No. 5 there was only a faint test for peptone and fair tests for the intermediate products. In the remaining flasks very good tests were obtained for the peptones and intermediate products. The amount of dissolved material and undigested residue is shown in the following table:

		Percentage of Meat Dissolved.	Percentage of Undigested Residue.
Flask No. 1.	Control.	93.00%	7.00%
Flask No. 2.	$1\frac{2}{3}$ Benzoate.	62.25%	37.75%
Flask No. 3.	2d Control.	94.10%	5.90%
Flask No. 4.	1% Benzoate.	55.65%	44.35%
Flask No. 5.	0.5% Benzoate.	83.25%	16.75%
Flask No. 6.	0.25% Benzoate.	91.30%	8.70%
Flask No. 7.	0.125% Benzoate.	90.30%	9.70%
Flask No. 8.	0.625% Benzoate.	90.90%	9.10%

This series in connection with the tests for the products of digestion shows that 1% or more of sodium benzoate is sufficient to prevent digestive action in this experiment; 0.5% materially retards digestive action; while 0.25% and less have but slight effect on digestion although the controls showed a slightly higher degree of efficiency.

In the following experiment an artificial gastric juice was made by removing the mucous membrane from the stomach of a dog. Forty grams of this was ground up in a mortar with 40 cc. of 1% acetic acid. After standing for a short time it was added to some chloroform water in the proportion of 40 to 100. After a few days it was strained through cloth and diluted with an equal volume of 0.2% hydrochloric acid and was then ready for use.

Dry fibrin was also used in this experiment because it is a proteid substance, easily digested and the lack of water in the fibrin gave more approximately accurate results in determining the undigested residues.

Experiment 7. Digestion continued for 18 hours at a temperature of 38 to 40 degrees C.

Flask No. 1. Control. 1 gram dry fibrin in 50 cc. water + 50 cc. gastric extract.
Flask No. 2. 1 gram fibrin + 50 cc. gastric extract + 1 gram sodium benzoate in 50 cc. water.
Flask No. 3. 1 gram fibrin + 50 cc. gastric extract + 0.5 gram sodium benzoate in 50 cc. water.
Flask No. 4. 1 gram fibrin + 50 cc. gastric extract + 0.25 gram sodium benzoate in 50 cc. water.
Flask No. 5. 1 gram fibrin + 50 cc. gastric extract + 0.125 gram sodium benzoate in 50 cc. water.
Flask No. 6. 1 gram fibrin + 50 cc. gastric extract + 0.0625 gram sodium benzoate in 50 cc. water.

The tests showed that no digestion took place in flasks 2 and 3. A trace of peptone was found in No. 4; a fair test in No. 5; a good test in No. 6 and the strongest in No. 1, the control. A small amount of hydrochloric acid was added to the contents of the flasks at intervals during digestion. Some cloudiness resulted in Nos. 2 and 3, when this was done, but the other flasks remained clear.

		Percentage of Fibrin Dissolved.	Percentage of Undigested Residue.
Flask No. 1.	Control.	81.10%	18.90%
Flask No. 2.	1% Benzoate.	......	plus 72 mg.
Flask No. 3.	0.5% Benzoate.	......	plus 23 mg.
Flask No. 4.	0.25% Benzoate.	17.60%	82.40%
Flask No. 5.	0.125% Benzoate.	52.10%	47.90%
Flask No. 6.	0.0625% Benzoate.	64.90%	35.10%

A glance at the table shows that in none of the benzoated flasks were the results as good as in the control; even with the smaller percentages of the benzoate, digestion had been materially retarded. In Nos. 2 and 3 the results show that there was absolutely no solution of the fibrin, but that at the end of the experiment there was an actual increase in weight. In the case of No. 2 there was a gain of 72 milligrams and in No. 3 of 23

milligrams. This gain in weight was undoubtedly due to some precipitation of benzoic acid when the gastric extract and solution of sodium benzoate were mixed and the precipitate remained upon the filter with the fibrin. The antiseptic action of sodium benzoate was also shown in this experiment. The flasks were allowed to stand 2 months. At the end of that time No. 1 showed a profuse fungus growth. There was some sediment in the bottom of No. 6 but the others were as clear as crystal.

Rennin. An experiment was also carried out to determine if the presence of sodium benzoate hindered in any way the action of the milk curdling enzyme of the stomach. For this purpose 25 grams of the mucous membrane of the fourth stomach of a sheep were removed. After trituration in the mortar with 25cc of 1% of acetic acid for a half an hour, 250cc of chloroform water were added and the whole was allowed to stand for two days. It was then neutralized with a solution of 1% sodium carbonate, strained and filtered and was then ready for use.

Experiment 8. In all cases the milk and sodium benzoate were mixed for an hour before adding the digestive extract. Temperature 38 degrees C.

Flask No. 1. Normal. 10 cc. milk.
Flask No. 2. Control. 10 cc. milk + 1 grain commercial rennin.
Flask No. 3. 2d Control. 10 cc. milk + 2 cc. of above extract.
Flask No. 4. 10 cc. milk + 1 gram sodium benzoate + 2 cc. extract = 10% sodium benzoate.
Flask No. 5. 10 cc. milk + 0.5 gram sodium benzoate + 2 cc extract = 5% sodium benzoate.
Flask No. 6. 10 cc. milk + 0.2 gram sodium benzoate + 2 cc. extract = 2% sodium benzoate.
Flask No. 7. 10 cc. milk + 0.1 gram sodium benzoate + 2 cc. extract = 1% sodium benzoate.
Flask No. 8. 10 cc. milk + 0.05 gram sodium benzoate + 2 cc. extract = 0.5% sodium benzoate.
Flask No. 9. 10 cc. milk + 0.02 gram sodium benzoate + 2 cc. extract = 0.2% sodium benzoate.
Flask No. 10. 10 cc. milk + 0.01 gram sodium benzoate + 2 cc. extract = 0.1% sodium benzoate.
Flask No. 11. 10 cc. milk + 0.005 gram sodium benzoate + 2 cc. extract = 0.05% sodium benzoate.

Within 15 minutes after the beginning of digestion moderately firm clots had formed in Nos. 2 and 3—the controls. At the end of 40 minutes some whey was forming in No. 2 and moderately firm clots were found in 9, 10 and 11. The contents of 4, 5, 6, 7 and 8 were still fluid. At the end of one hour and 40 minutes, clots appeared in Nos. 7 and 8 and some whey was showing in those which had previously clotted. After 5 hours a soft clot appeared in No. 6. Nos. 4 and 5 were still fluid. The normal milk in No. 1 had undergone no change. The flasks were put in the incubator over night at a temperature of 40 degrees C. In the morning the clots had contracted still more and there was a greater abundance of whey, especially in the controls 2 and 3. In 9, 10 and 11 the clots were a little larger than in the controls. In 6, 7 and 8 the clots were still larger and irregular and a smaller quantity of whey. Nos. 4 and 5 were still fluid. In No. 1 the normal milk had undergone the natural process of souring. In Nos. 4 and 5 there was sufficient sodium benzoate present to inhibit the action of the enzyme rennin and was also sufficiently antiseptic to prevent the natural souring of the milk.

Another control experiment was carried out by boiling some of the rennin extract from the sheep's stomach and adding 2 cc. of it to 10 cc. of milk as in No. 3. Observations were carried on for 2½ hours but there was no evidence of clotting, showing that the boiling had killed the enzyme. The flask was then put in the incubator for over night and in the morning it was found to have undergone the natural process of souring. In none of the benzoate flasks did the clots form as quickly as in the controls. Sodium benzoate to the extent of 0.2% or less appeared to have but slight effect on the action of rennin; 0.5% to 1% materially retarded its action and 2% very nearly prevented any clotting. 5% and 10% inhibited clotting altogether.

Experiment 9. In this experiment commercial rennin was used in the form of tablets, each tablet containing 1 grain of rennin.

Flask No. 1. Control. 10 cc. milk + 1 grain rennin.

Flask No. 2. 10 cc. milk + 1 gram sodium benzoate + 1 grain rennin = 10% benzoate.

Flask No. 3. 10 cc. milk + 0.5 gram sodium benzoate + 1 grain rennin = 5% benzoate.

Flask No. 4. 10 cc. milk + 0.2 gram sodium benzoate + 1 grain rennin = 2% benzoate.

Flask No. 5. 10 cc. milk + 0.1 gram sodinm benzoate + 1 grain rennin = 1% benzoate.

Flask No. 6. 10 cc. milk + 0.05 gram sodium benzoate + 1 grain rennin = 0.5% benzoate.

Flask No. 7. 10 cc. milk + 0.02 gram sodium benzoate + 1 grain rennin = 0.2% benzoate.

Digestion was allowed to continue for half an hour at 36 to 37 degrees C. At the end of that time it was found that firm clots had formed in Nos. 1, 5, 6 and 7, the others remaining fluid. The flasks were put in the incubator over night and examined again the next morning. In 1, 5, 6 and 7 the clots were cylindrical and well formed ; considerably contracted and a large proportion of whey was present. In No. 4 there was an irregular mass at the bottom of the flask with some whey around it. In Nos. 2 and 3 there were some irregular masses at the top and bottom of the milk as if there had been some attempt at clotting. The result was best in the control for here was the smallest clot and the greatest amount of whey. As compared with the preceding experiment each flask in the last experiment undoubtedly contained a larger amount of rennin, and this helps to explain why clotting might occur within half an hour in the presence of sodium benzoate to the extent of 1%.

Pancreatic Digestion. Experiments were made with all of the enzymes of the pancreas e. g. amylopsin, trypsin, steapsin and milk curdling.

Amylopsin. This enzyme was studied by preparing an alkaline solution of pancreatin as follows : Pancreatin 5 grams, Sodium Carbonate 10 grams, Distilled Water sufficient to make 1000 cc.

Experiment 10. In this experiment digestion was allowed to continue for three hours at a temperature of 41 degrees C., the starch having previously been boiled in the water.

Flask No. 1. Control. 2½ grams starch + 60 cc. water + 30 cc. pancreatin solution.

Flask No. 2. 2½ grams starch + 60 cc. water + 30 cc. pancreatin solution + 1 gram sodium benzoate in 30 cc. water.

Flask No. 3. 1 gram starch + 50 cc. water + 25 cc. pancreatin solution + 2 grams sodium benzoate in 50 cc. water.

Flask No. 4. 2d Control. 1 gram starch + 50 cc. water + 25 cc. pancreatin solution + 25 cc. water.

Flask No. 5. 1 gram starch + 50 cc. water + 25 cc. pancreatin solution + 1 gram sodium benzoate in 25 cc. water.

Flask No. 6. 1 gram starch + 50 cc. water + 25 cc. pancreatin solution + 0.5 gram sodium benzoate in 25 cc. water.

Flask No. 7. 1 gram starch + 50 cc. water + 25 cc. pancreatin solution + 0.25 gram sodium benzoate in 25 cc. water.

Flask No. 8. 1 gram starch + 50 cc. water + 25 cc. pancreatin solution + 0.125 gram sodium benzoate in 25 cc. water.

Quantitative tests with Fehling's solution gave the following results :

		Number of cc. of solution equal to 0.05 gram sugar or to reduce 10 cc. Fehling's.
Flask 1.	Control.	4. cc.
Flask 2.	$\frac{5}{6}$% Benzoate.	5.3 cc.
Flask 3.	1.6% Benzoate.	10.4 cc.
Flask 4.	2d Control.	10.5 cc.
Flask 5.	1% Benzoate.	11.0 cc.
Flask 6.	0.5% Benzoate.	9.7 cc.
Flask 7.	0.25% Benzoate.	10.1 cc.
Flask 8.	0.125% Benzoate.	9.9 cc.

It will be noted that in flasks 1 and 2 where there was 2½ times as much starch present as in the other flasks, the greatest amount of sugar was found whether sodium benzoate was present or not, but such difference as there is, is in favor of the normal. With regard to the remaining flasks with the smaller quantity of starch, there is proportionately less sugar and it would be difficult to determine from the results that the benzoate had any special effect, except perhaps to slightly favor the digestion ; because with the exception of No. 5, all of the others from 3 to 8 inclusive show that slightly more sugar was produced in the benzoated flasks than in the 2nd control. The difference is so slight however, that it may well come within the limits of error.

Trypsin. Experiment 11. This experiment was concerned with the pancreatic digestion of proteids. A solution of pancreatin was prepared as described for Experiment 10. Raw meat was used for the proteid. Digestion continued for 15½ hours.

Flask No. 1. Control. 2 grams meat + 30 cc. water + 30 cc. pancreatin solution.
Flask No. 2. 2 grams meat + 30 cc. pancreatin solution + 1 gram sodium benzoate in 30 cc. water.
Flask No. 3. 2d Control. 2 grams meat + 50 cc. water + 50 cc. pancreatin solution.
Flask No. 4. 2 grams meat + 50 cc. pancreatin solution + 1 gram sodium benzoate in 50 cc. water.
Flask No. 5. 2 grams meat + 50 cc. pancreatin solution + 0.5 gram sodium benzoate in 50 cc. water.
Flask No. 6. 2 grams meat + 50 cc. pancreatin solution + 0.25 gram sodium benzoate in 50 cc. water.
Flask No. 7. 2 grams meat + 50 cc. pancreatin solution + 0.125 gram sodium benzoate in 50 cc. water.
Flask No. 8. 2 grams meat + 50 cc. pancreatin solution + 0.0625 gram sodium benzoate in 50 cc. water.

Peptones and intermediate products were found in all of the flasks. The strongest tests for peptones, however, were obtained from flasks 2 and 4.

		Percentage of Meat dissolved.	Percentage of Undigested Residue.
Flask No. 1.	Control.	83.85%	16.15%
Flask No. 2.	$1\frac{2}{3}$ Benzoate.	83.55%	16.45%
Flask No. 3.	2d Control.	92.40%	7.60%
Flask No. 4.	1% Benzoate.	86.65%	13.35%
Flask No. 5.	0.5% Benzoate.	92.95%	7.05%
Flask No. 6.	0.25% Benzoate.	90.50%	9.50%
Flask No. 7.	0.125% Benzoate.	92.60%	7.40%
Flask No. 8.	0.0625% Benzoate.	89.15%	10.85%

In Nos. 1 and 2 the results are nearly the same. In the series 3 to 8 inclusive there is greater variation. In this series there was a greater amount of the pancreatin solution present—about 40% more, which undoubtedly accounts for the higher percentages of the meat dissolved. In Nos. 3, 5 and 7, the figures compare very closely and although there is more difference between the remaining figures, the inference may be justified, in connection with the peptone tests, that the benzoate did not materially hinder the digestion of the meat.

Experiment 12. In this case dry fibrin was used in connection with an extract made from the pancreas of a horse. Digestion for 18 hours. In all cases the fibrin was allowed to soak in the sodium benzoate solution for three hours before the pancreatic extract was added and digestion begun.

Flask No. 1. Control. 1 gram fibrin + 50 cc. water + 50 cc. pancreatic extract.
Flask No. 2. 1 gram fibrin + 50 cc. pancreatic extract + 1 gram sodium benzoate in 50 cc. water.
Flask No. 3. 1 gram fibrin + 50 cc. pancreatic extract + 0.5 gram sodium benzoate in 50 cc. water.
Flask No. 4. 1 gram fibrin + 50 cc. pancreatic extract + 0.25 gram sodium benzoate in 50 cc. water.
Flask No. 5. 1 gram fibrin + 50 cc. pancreatic extract + 0.125 gram sodium benzoate in 50 cc. water.
Flask No. 6. 1 gram fibrin + 50 cc. pancreatic extract + 0.0625 gram sodium benzoate in 50 cc. water.

Good peptone tests were obtained from all the flasks.

		Percentage of Fibrin dissolved.	Percentage of Undigested Residue.
Flask No. 1.	Control.	56.00%	44.00%
Flask No. 2.	1% Benzoate.	55.50%	54.50%
Flask No. 3.	0.5% Benzoate.	51.10%	48.90%
Flask No. 4.	0.25% Benzoate.	53.10%	46.90%
Flask No. 5.	0.125% Benzoate.	52.50%	47 50%
Flask No. 6.	0.0625% Benzoate.	60.80%	39.20%

The results show that digestion was not prevented in any of the flasks, as demonstrated by the peptone tests. From the amount of fibrin dissolved, it would appear that the benzoate retarded digestion in all but No. 6, where the very slight amount present apparently favored digestion. The contents of the flasks were kept one month after making the digestive tests in order to note any antiseptic effects of the benzoate. At the end of the month all of the flasks had a putrefactive odor and there was some scum or sediment in each, indicating that sodium benzoate was not as efficient as an antiseptic in an alkaline medium as in the acid gastric experiments already noted.

Milk Curdling Enzyme. Experiment 13. The milk curdling enzyme of the pancreas was experimented with in this case. A small piece of dog pancreas was placed in each flask with the milk, and although it was questionable if the other pancreatic enzymes would not overshadow the action of any milk curdling enzyme, the work was carried through although somewhat unsatisfactory in results.

Flask No. 1.	Control. 10 cc. milk + a small piece of fresh pancreas.						
Flask No. 2.	10 cc. milk	+ 1	gram	sodium	benzoate	+	pancreas.
Flask No. 3.	10 cc. "	+ 0.5	"	"	"	+	"
Flask No. 4.	10 cc. "	+ 0.2	"	"	"	+	"
Flask No. 5.	10 cc. "	+ 0.1	"	"	"	+	"
Flask No. 6.	10 cc. "	+ 0.05	"	"	"	+	"
Flask No. 7.	10 cc. "	+ 0.02	"	"	"	+	"

The contents of the flasks were allowed to digest for 2 hours at 36 to 37 degrees C, with no apparent change. The flasks were then put in the incubator over night. The next morning the cream had risen to the surface in all. In No. 1 there was a mass of cream and the piece of pancreas at the top, and some whey-like liquid below. In No. 7 the conditions were similar but not so marked. In No. 6 the pancreas was suspended in the fluid and there was but a slight separation of the whey-like fluid. In No. 5 the pancreas was at the bottom and but a mere trace of whey. In 2, 3 and 4 the pancreas was also at the bottom and the fluid was of a uniformly milky appearance. It appeared as if tryptic digestion had gone on simultaneously and this was shown to be the fact; for on making the peptone test peptones were found in all flasks except No. 2 in which they were entirely absent. and in No. 3 in which only a very faint trace was obtained.

The inference formed from this experiment was that 0.2% of sodium benzoate caused but slight interference with any milk curdling action, but that more than that amount inhibited it. With regard to the tryptic digestion of milk, 2% of sodium benzoate did not materially interfere, 5% caused marked retardation and 10% entirely inhibited it.

Experiment 14. This experiment was introduced in order to obtain, if possible, a purer milk curdling action without special interference of the other emzymes. Thirty grams of the pancreas of a sheep were triturated in a mortar with the addition of 150 cc. of brine. The mixture was allowed to stand for a day or two with occasional stirring. The reaction became slightly acid; this was overcome or neutralized with 1% sodium carbonate. The mixture was then strained and filtered.

Flask No. 1. Normal. 10 cc. milk.
Flask No. 2. Control. 10 cc. milk — 2 cc. brine solution.

Flask No. 3. 2d Control. 10 cc. milk + 1 grain rennin.

Flask No. 4. 3d Control. 10 cc. milk + 2 cc. brine extract of pancreas.

Flask No. 5. 10 cc. milk + 1 gram sodium benzoate + 2 cc. pancreas extract = 10% sodium benzoate.

Flask No. 6. 10 cc. milk + 0.5 gram sodium benzoate + 2 cc. pancreas extract = 5% sodium benzoate.

Flask No. 7. 10 cc. milk + 0.2 gram sodium benzoate + 2 cc. pancreas extract = 2% sodium benzoate.

Flask No. 8. 10 cc. milk + 0.1 gram sodium benzoate + 2 cc. pancreas extract = 1% sodium benzoate.

Flask No. 9. 10 cc. milk + 0.05 gram sodium benzoate + 2 cc. pancreas extract = 0.5% sodium benzoate.

Flask No. 10. 10 cc. milk + 0.02 gram sodium benzoate + 2 cc. pancreas extract = 0.2% sodium benzoate.

Flask No. 11. 10 cc. milk + 0.01 gram sodium benzoate + 2 cc. pancreas extract = 0.1% sodium benzoate.

Flask No. 12. 10 cc. milk + 0.005 gram sodium benzoate + 2 cc. pancreas extract = 0.05% sodium benzoate.

After digesting 5 minutes in the incubator at a temperature of 38 degrees C. it was found that numbers 1, 2 and 5 were still fluid, while numbers 4 and numbers 6 to 12 inclusive showed moderately firm clots. In No. 3 the clot was very firm. Ten minutes later there was no further change. After thirty minutes from the beginning of the experiment No. 5 clotted. One hour and a half from the beginning of the experiment numbers 4, 9, 10, 11 and 12 lost the coagulated condition and became quite fluid again, indicating the beginning of tryptic digestion. Nos. 5, 6, 7 and 8 were still clotted. Five and a half hours from the beginning of the experiment the normal and control flasks, Nos. 1 and 2, were still fluid having undergone no change; numbers 5 and 6 were a little firmer than the others, except No. 3, in which there was a good clot and considerable whey. The flasks were all put in the incubator over night. In the morning it was found that No. 1 (normal) had undergone natural souring. No. 2 was apparently the same as the day before, the brine solution having probably prevented the souring. In No. 3 the clot had become much contracted and there was considerable whey. In Nos. 4 to 12 inclusive—the flasks containing the pancreatic extract—tests were made and peptones were found to be present in all, showing that tryptic digestion had not been prevented. The presence of

sodium benzoate to the extent of 10% did not prevent clotting, but delayed it for 30 minutes, nor did it prevent tryptic digestion.

A control experiment was introduced by boiling some of brine extract of the pancreas to destroy the enzymes. 2 cc. of this boiled extract were added to 10 cc. of milk and the flask kept as the others had been. After 2½ hours no changes were observed. The flask was then kept in the incubator over night, but no further changes were observable. There was no evidence of clotting and no peptones were found.

Steapsin. The fat splitting enzyme of the pancreas which plays such an important part as an aid in the emulsification of fats was used in the following experiment by placing a piece of fresh pancreas of a dog in some neutral fat (cream) which had been colored with litmus solution. The cream was found to be of neutral reaction as was also the sodium benzoate. When the litmus solution was mixed with the cream a neutral or light blue color resulted. If the steapsin was active and the fat acted upon by it, then the neutral or blue color of the mixture would be changed to a red on account of the presence of fatty acids formed by the action of steapsin upon the fat of the cream, splitting it up into fatty acids and glycerine.

Experiment 15.

Flask No. 1. Normal. 1 cc. cream + 1 cc. litmus solution + 1 cc. water.

Flask No. 2. Control. 1 cc. cream + 1 cc. litmus solution + 1 cc. water + small piece of pancreas.

Flask No. 3. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 10% sodium benzoate = 1—30 of sodium benzoate.

Flask No. 4. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 5% sodium benzoate = 1—60 sodium benzoate.

Flask No. 5. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 2.5% sodium benzoate = 1—120 sodium benzoate.

Flask No. 6. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 1% sodium benzoate = 1—300 sodium benzoate.

Flask No. 7. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 0.5% sodium benzoate = 1—600 sodium benzoate.

Flask No. 8. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 0.25% sodium benzoate = 1—1200 sodium benzoate.

Flask No. 9. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 0.125% sodium benzoate = 1—2400 sodium benzoate.

Flask No. 10. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 0.0625% sodium benzoate = 1—4800 sodium benzoate.

Flask No. 11. Pancreas + 1 cc. cream + 1 cc. litmus + 1 cc. 0.03125% sodium benzoate = 1—9600 sodium benzoate.

The cream, litmus and sodium benzoate were all mixed together and allowed to stand for 2½ hours before adding the pancreas. The flasks were kept in the incubator at 37 degrees C. and were observed at intervals. A red color soon appeared in the litmus surrounding the pancreas. Within twenty minutes this had appeared in all the flasks but the normal—No. 1. The red color was best developed in Nos. 2 and 8. In No. 3 there was some fatty acid as shown by a slight red, but this flask was the poorest of the series. Nos. 4, 5, 6 and 7 did not show much difference between themselves but all were better than No. 3. No. 8 was nearly as good as No. 2. There was not much difference between Nos. 9, 10 and 11 but none of them were as good as No. 8, although they were slightly better than 4 to 7 inclusive. They were all left in the incubator over night and examined the next morning when it was found that the best development of fatty acids had occurred in Nos. 2, 8, 9, 10 and 11 ; Nos. 6 and 7 were next in order, while 3, 4 and 5 were the poorest of the series. No. 1 had also turned red on account of the development of the acids incident to the natural souring of cream. It would appear, therefore, that the presence of sodium benzoate in proportion of 1 to 1200 did materially affect the action of steapsin. In the proportion of 1 to 300 and 1 to 600 the action was somewhat retarded. The action was still more retarded by the proportion of 1 to 120 and 1 to 60 ; but 1 to 30 did not stop the action of the enzyme.

Two other tests were carried out with a larger proportion of sodium benzoate present. In these tests the ingredients were all mixed together at the same time.

Flask No. 12. Pancreas + 1 cc. cream + 1 cc. litmus + 5 cc. 10% sodium benzoate = 1 to 14 of sodium benzoate.

Flask No. 13. Pancreas + 1 cc. cream + 1 cc. litmus + 5 cc. water + 1 gram sodium benzoate = 1 to 7 of sodium benzoate.

In No. 12 there was a slight evidence of fatty acid in 20 minutes. Two hours later this was somewhat increased, and there

was a faint trace of red color in No. 13. After remaining in the incubator over night there was not much change. On shaking the flasks No. 12 became slightly red while No. 13 remained blue, although some red was present around the piece of pancreas itself, indicating traces of fatty acids, but these were not strong enough to overcome the blue color.

Another control was prepared by placing a piece of the pancreas in some litmus and water. This was left in the incubator over night. In the morning it was found that no change had occurred.

Invertin. A study was also made of the action of the enzyme of the succus entericus (intestinal juice). A preparation was made by removing 40 grams of the mucous membrane of the small intestine of a dog; triturating it in a mortar with 40 cc. of 1% acetic acid and then adding 400 cc. of chloroform water. After standing for two days this mixture was made slightly alkaline by the addition of sodium carbonate. This enzyme had the power of converting cane sugar into dextrose a reducing sugar. The cane sugar was tested before the experiment began and was found to be free from any reducing sugar.

Experiment 16.

Flask No. 1. Check. 50 cc. 2% cane sugar + 50 cc. water.
Flask No. 2. Control. 50 cc. cane sugar + 25 cc. water + 25 cc. intestinal extracts.
Flask No. 3. 50 cc. 2% cane sugar + 25 cc. extract + 1 gram sodium benzoate in 25 cc. water.
Flask No. 4. 50 cc. 2% cane sugar + 25 cc. extract + 0.5 gram sodium benzoate in 25 cc. water.
Flask No. 5. 50 cc. 2% cane sugar + 25 cc. extract + 0.25 gram sodium benzoate in 25 cc. water.
Flask No. 6. 50 cc. 2% cane sugar + 25 cc. extract + 0.125 gram sodium benzoate in 25 cc. water.
Flask No. 7. 50 cc. 2% cane sugar + 25 cc. extract + 0.0625 gram sodium benzoate in 25 cc. water.

The solutions of sugar and sodium benzoate were mixed together and allowed to stand over night before the digestive extract was added. Digestion was continued 6 hours; the temperature at the outset being 30 degrees C. and rising toward the end of the experiment to 42° C.

		Number of cc. of solution equal to 0.05 gram sugar or to reduce 10 cc. Fehling's.
Flask No. 1.	Check.	No reduction.
Flask No. 2.	Control.	37 cc.
Flask No. 3.	1% Benzoate.	44 cc.
Flask No. 4.	0.5% Benzoate.	42 cc.
Flask No. 5.	0.25% Benzoate.	37.3 cc.
Flask No. 6.	0.125% Benzoate.	24.8 cc.
Flask No. 7.	0.0625% Benzoate.	35.4 cc.

Qualitative tests 1 hour after digestion began showed the presence of reducing sugar in flasks 2, 5, 6 and 7, and after another hour reducing sugar was found in all of them. The quantitative tests indicate that the presence of sodium benzoate to the extent of 0.25% does not affect the conversion of cane sugar into reducing sugar; but that 0.5% and 1% materially retarded the action of the enzyme.

SUMMARY.

CARBOHYDRATES. The experiments indicate that the digestion of carbohydrates, starch and cane sugar, was not much interfered with on account of the presence of sodium benzoate. When the benzoate was present to the extent of 0.5% to 1% there was some evidence that digestion was delayed. In smaller percentage 0.25% or less the digestion, as a rule, seemed to be normal. This statement applies, in general, to the action of the enzymes ptyalin of the saliva, amylopsin of the pancreatic juice, and invertin of the succus entericus.

PROTEIDS. In the digestion of egg albumin and raw meat with solutions of pepsin in hydrochloric acid, 1% of sodium benzoate was sufficient to altogether inhibit the action of the enzyme; 0.5% did not quite inhibit digestion but very materially retarded it; 0.25% and less did not interfere with the digestion of egg albumin but did retard it slightly in the case of the meat. In the experiment with the extract made from the mucous membrane of the dog's stomach, and fibrin as the proteid to be digested, still more unfavorable results were obtained; one-half per cent of the benzoate entirely prevented digestion; 0.25% permitted only a trace of digestion, and a percentage as low as

0.0625% materially retarded the action of the enzyme. The digestive fluid in this case contained the pepsin fresh from the gastric mucous membrane and the conditions of the experiment should be regarded as more nearly comparable to normal than where merely a solution of pepsin is used.

In the digestion of proteids with the pancreatic preparations, sodium benzoate up to 1% and $1\frac{2}{3}$% did not prevent the formation of peptones, although 1% retarded digestion in the case of raw meat in a solution of the pancreatin, while in the artificial extract of the pancreas of a horse with dry fibrin as the proteid 0.5% retarded digestion somewhat, while lower percentages had only a slight effect in this direction. In an experiment on milk it was found that sodium benzoate to the extent of 10% inhibited the formation of peptones and that 5% permitted only a faint trace of them. Two per cent and less of sodium benzoate apparently did not materially interfere with the production of peptones. In another experiment upon milk, in which a brine extract of the pancreas was used, sodium benzoate to the extent of 10% did not prevent the formation of peptones.

Rennin. In the preparation of rennin made from the fourth stomach of a sheep the presence of sodium benzoate to the extent of 0.05% to 0.2% delayed the curdling of the milk for 20 to 25 minutes. Five per cent. and ten per cent. of the benzoate prevented the curdling altogether and 0.5% to 2% very materially retarded the process.

In another experiment in which commercial rennin, in tablet form was used, sodium benzoate to the extent of 0.2% to 1% did not seem to materially interfere with the curdling of the milk. Even as high an amount as 10% did not inhibit in this case, but caused an irregular mass to form in the milk as if there had been an attempt at curdling. The same results were found in the tubes containing 2% and 5% of the benzoate.

Of these two rennin experiments the first is more nearly in accord with normal conditions and should be considered the more reliable.

The presence of a milk-curdling enzyme in the pancreas is questioned by some. Experiments were, nevertheless, tried in this direction, and although the results were not so satisfactory

as in the case of the gastric and commercial rennin there appeared to be some evidence of a curdling action. In the former case, pepsin did not interfere with the action of the rennin because pepsin does not work in a neutral or alkaline medium. Trypsin is active in a neutral or alkaline medium and therefore interfered more or less with the action of any milk-curdling enzyme that might have been present.

In the experiment in which a small piece of pancreas was placed directly into the milk the results were unsatisfactory from a milk-curdling standpoint. No curdling took place after two hours observation. After digestion over night in the incubator no satisfactory clots were found, although there appeared to be a whey-like fluid in some of the tubes. On the basis of this whey-like fluid, 0.2% sodium benzoate, as compared with the normal, interfered somewhat with the production of this fluid. More than 0.2% inhibited this action. Peptones were also found in these tubes, so that assuming an interference on the part of the enzyme trypsin, it is somewhat questionable if a true milk-curdling action occurred.

More satisfactory results were obtained in using a brine extract from the pancreas of the sheep. In this case moderately firm clots were found in certain of the tubes within 5 minutes after the beginning of digestion. Later the coagulation disappeared and the milk apparently underwent digestion by the trypsin as shown by the presence of peptones. That the coagulation was not in any way due to the brine solution is shown by the fact that control No. 2 which contained milk and brine only remained fluid throughout the experiment. As much as 10% sodium benzoate did not prevent the coagulation but delayed it for 30 minutes. The brine extract apparently hastened the action of the milk-curdling enzyme or delayed the action of the trypsin ; for in this experiment there was good evidence of the activity of both enzymes.

Fat. The enzyme which has most to do with this food substance is steapsin which is developed in the pancreas. Steapsin is a most important factor in promoting the emulsification of fats. Sodium benzoate in the proportion of 1 to 1200 or about 0.08%, or less amounts did not appear to materially affect the

action of steapsin. In the proportion of 1 to 600 (0.16%) or 1 to 300 (0.33%) the action was somewhat retarded. Higher percentages caused still more retardation; but a proportion as high as 1 to 7 (14%) did not quite inhibit the action of the enzyme.

The presence of sodium benzoate to the extent of 0.2% did not appear to interfere with the digestion of carbohydrate food. Higher amounts did not always interfere; but in some cases they did retard the action of the enzymes, and the percentage above mentioned may be regarded as being within safe limits.

Sodium benzoate seemed to exert a more direct inhibitory action upon pepsin than any of the other enzymes studied. Although 0.2% of sodium benzoate did not interfere with the digestion of egg albumin, as little as 0.06% did materially retard the digestion of fibrin. The nature of the proteid may have some influence upon its digestibility in the presence of sodium benzoate.

The digestion of proteids, in the presence of sodium benzoate, by the pancreatic enzyme trypsin, was more readily accomplished than by pepsin. This was shown by the fact that 1% sodium benzoate usually inhibited the action of pepsin, while trypsin was still able to produce peptones in the same percentage of benzoate.

With 0.2% and less of the benzoate there was practically no injurious effect upon the trypsin. The nature of the proteids, as already mentioned, may have some influence upon their rate of digestion with sodium benzoate. In one experiment with milk, 5% of the benzoate permitted a faint trace of peptones. In another, 10% did not completely inhibit their production, while 2% apparently did not interfere with the digestion of the milk proteid.

The enzyme rennin, as prepared from the mucous membrane of the stomach, was found to be quite sensitive to the presence of sodium benzoate. The lower percentages (0.1%) retarded the action of the enzyme, while 5% and over completely inhibited it.

With regard to the milk-curdling enzyme of the pancreas, sodium benzoate also caused a retarding effect, but not so marked as in the case of the gastric enzyme.

Steapsin, the fat splitting enzyme of the pancreas, was mod-

erately sensitive to sodium benzoate; 0.08% or less of the benzoate did not appear to interfere with its action. Higher percentages caused some retardation, but as high a proportion as 1 to 7 (14%) of the benzoate did not cause complete inhibition.

Sodium benzoate caused less interference with digestion in a neutral or alkaline medium than in an acid medium.

From the evidence of the experiments it seems reasonable to conclude that the presence of sodium benzoate to the extent of 0.1% or less exercised no specially harmful effects upon the digestive enzymes. A higher percentage than this, in some cases, did retard the digestive processes, and a continuation of such condition might, in time, effect the general health of the individual.

It should be remembered, however, that in natural digestion the benzoate, mixed with the food, passes from the action of one digestive fluid to that of another. The benzoate, having been first concerned in the alkaline salivary digestion, may, as a result, produce a less profound effect upon peptic digestion than in the conditions of the experiments where the benzoate was introduced *de novo* in each digestive fluid.

EXPERIMENTS WITH NUCLEIN.

LEE SELDON BACKUS

It has long been known that all animal or vegetable substances are made up of histologic units known as cells ; that these cells possess the power to develop and reproduce themselves and the constituent which makes this possible is the nuclein which they contain. Chemically the nucleins are complex proteid bodies, notable for their large amount of phosphorus.

Quite recently it has been found possible to separate this nuclein from the other substances contained in the cell body, and in view of the important function which it normally performs it was thought that it might perhaps have important therapeutic effects as a tonic to the system and by increasing natural resistance to disease.

Nuclein is present in, and obtainable from, a number of sources. The thyroid glands, liver, kidneys, lungs, testes, ovaries, spermatozoa, brain, spinal cord, etc., have all been examined chemically with the result that nuclein has been found to be the most abundant as well as the most important proteid substance present.

It has not been found advisable, however, to obtain the nuclein from any of the above sources. It has been found that it can be most easily derived from the yeast plant and is put on the market both in the form of a solution and in tablets. As seen in solution it is a reddish brown liquid, slightly saline taste, with an odor not unlike that of beef boullion, and of neutral reaction.

As a therapeutic agent, although it has some antiseptic power, it is supposed to act by multiplying and stimulating the natural resisting forces or the phagocytes. Such a physiologic action would refer us at once to morbid blood states and their consequences. Such defects generally being due to blood toxicity. The former includes impoverished conditions of the blood in which the circulating fluid is lacking in those qualities which

are necessary to the performance of its proper functions. Nuclein is also claimed to be indicated wherever cell integrity and cell activity are lacking, whether due to insufficient reinforcement from the blood or to inhibition of toxins residing in the blood. And likewise in such conditions of toxicity in which the system has been invaded by pathogenic germs and the defensive proteids find themselves impotent to meet functional demands in consequence of systemic infection, and it is in the hope of gaining some insight as to the real therapeutic value of nuclein that the following experiments have been conducted. With only a small number of animals (all of which were dogs) and the length of time for experimenting necessarily limited, the results are not fully conclusive, but might serve a useful purpose, as a hint, in further investigation along the same line.

As the white blood corpuscles are among the most active of the phagocytes, and the primary action of nuclein is the supposedly rapid increase of these bodies, most of the examinations have been upon the blood. In some cases both red and white cells were counted. In these cases dilution was made with Toisson's fluid, using Thoma's apparatus. Where only the leucocytes were counted a ⅓% acetic acid solution was used. In every case one hundred squares were counted for the red corpuscles and the entire field for the white. In any count if anything happened which might cause an error, the preparation was discarded and a new one prepared.

In getting an estimation of the hemoglobin Tallquist's hemoglobinometer was used.

I found it most convenient to obtain the blood from the inside of the ear, selecting a spot void of hair and puncturing with a sharp lancet one of the small vessels which can be readily seen through the integument in this part.

In preparing to make a count, the ear is first washed with water, then wiped off with alcohol and dried. A quick thrust of the lancet brings the blood, the first drop being discarded and the succeeding used. It is well to have an assistant to keep the animal quiet at this stage, as a slight jerk of the head may easily cause a failure in filling the pipette. Having obtained the required amount of blood, the end of the pipette is wiped off, then

immediately filled with the diluting fluid and revolved for one minute, holding the pipette in a horizontal position. This serves to thoroughly distribute the corpuscles. A drop of suitable size is then placed upon the counting chamber, the cover glass placed over it and the preparation examined.

The first case on which we used nuclein and which was accurately recorded entered the College Clinic October 30th.*

The animal was a male collie, six months old, and weighing about fifty pounds. The history of the case, as given by the owner, was that the dog had been running about the house and barn and went under the latter in the afternoon of September 15th. As he failed to come out by the following morning, some boards in the barn floor were raised and the animal was taken out of a privy pit, covered with the filth. The dog was washed and given good care but did not appear normal. In a few days he began to show symptoms of paralysis in the right hind leg and in two weeks the paralysis had extended to the opposite side and he was then brought in for treatment

As seen by us on October 30th there was paraplegia, extreme nervousness, and the head kept drawn toward the right side. When disturbed by being handled, as in giving medicine, the dog would suddenly give two or three turns and then, bringing the head down against the bedding with a quick jerk, would lie quiet for a time.

The first blood count, 4 P. M., October 30th, resulted as follows: Erythrocytes 5,000,000; Leucocytes 4,900.

This shows a normal count for the red cells but a marked deficiency in the white; the normal for the dog being about 10,000. As soon as the blood was taken for this count, twenty minims of nuclein were injected hypodermically.

At 4:30 P. M.: Red cells, 5,628,000; White, 6,402.

At 5:30 P. M.: " " 5,620,000; " 8,444.

In addition to the nuclein treatment, which consisted of 20 minims three times daily, he was given a laxative of calomel gr. ss., sodium bicarbonate gr. ss. Also mixed treatment, two tablets thrice daily, then twice daily.

---

*Published as Case Report "Canine Toxemia," Amer. Vet. Review, Nov. 1906. XXX-966.

No. 1 :

Strych, Arsenate,		$\frac{16}{67}$ grains
Quinine "		1 grain
Echinacea Ext.		16 grains
Glycerine		
Water	aa q. s.	2 ounces

M. Sig. Teaspoonful twice daily for three days, then thrice daily.

The laxatives which were given caused a slight movement of the bowels.

On November 2nd a blood count was made showing Erythrocytes 6,000,000, Leucocytes 6,000.

November 4th omitted treatment No. 1 and substituted tablets of digitalis and aconite—one tablet three times daily.

November 6th. Red cells 6,880,000, White cells 7,500.

November 9th. An abscess was found under the integument in front of the shoulder. The hair was sheared from the red, fluctuating swelling and slight pressure sufficed to break it. There was discharged a thin bloody pus from which a smear was made and examined microscopically. Rod-like organisms were found, each bearing a capsule.

November 10th. Up to this time the patient had been fed milk from a bottle in the form of a drench, about two ounces three times daily. On this date he seemed in better spirits and was able to use the legs to a limited extent and lapped some milk from a basin. He also ate a dog biscuit with apparent relish. Leucocytes 9,000. One dram of nuclein was given once daily by hypodermic injections from now on. The mixed treatment was dropped and a small dose of Epsom salts was given.

November 12th another abscess was ruptured on the right abdominal wall and an organism similar to the one found on the ninth was isolated. Every day or two an enema of warm water was given which usually resulted in the free passage of feces mixed with hay which the dog had eaten from his bed.

On November 15th an examination of the urine was made with the following results :

Specific gravity	1030
Urea	39 grams per 1000 cc.
Albumin	None
Sugar	None
Phosphates	2.6 grams per 1000 cc.
Chlorides	.94 grams per 1000 cc.

Beginning November 20th one dram of nuclein was given twice daily by mouth.

December 2nd. The dog had continued to improve and could now walk, though with some difficulty. As there was extreme nervousness bromide was given to quiet him.

On December 10th the dog was led outside for a little exercise which appeared to be of much benefit. The nuclein was now reduced to one-half dram twice daily.

December 20th. Red cells 6,000,000, White cells 12,500.

On December 23rd he was thought to be sufficiently convalescent to be discharged and went home.

The following table shows the pulse and temperature while undergoing treatment:

DATE.	PULSE.	TEMPERATURE.
Oct. 30, '05	120	102.5
Oct. 30, '05, (4 P. M.)	130	102.5
Oct. 31, '05	120	102.4
Nov. 1, '05	120	102.0
Nov. 2, '05	120	102.6
Nov. 3, '05	130	104.0
Nov. 4, '05	——	101.5
Nov. 6, '05	——	102.7
Nov. 7, '05	——	103.0
Nov. 8, '05	120	103.4
Nov. 9, '05	——	102.4
Nov. 10, '05	——	102.5
Nov. 12, '05	——	103.0
Dec. 2, '05	——	103.0

On January 9th the case was returned. While away there had been a rapid increase in flesh but otherwise he was much the same as when first brought to the clinic. Head drawn to the right side, rolling over and over when excited, and appearing to suffer greatly. He was put on treatment of triple arsenates, with nuclein and mixed treatment. As there was not much improvement shown it was thought best that the animal be chloroformed and a post-mortem held. This took place January 15th. A blood count was made January 7th and showed leucocytes 9,000.

Autopsy. Lungs—right anterior lobe two-thirds hepatized; principal and middle lobe entirely hepatized; both lobes of the

left lung were congested approaching hepatization. Heart—right auricle in diastole ; valves and heart muscle normal ; left heart in systole ; thoracic cavity normal. Liver—congested ; bile cyst well filled and normal in appearance. Spleen normal. Stomach filled with gas. Small intestines normal. Large intestines normal and filled with semi-dry dark green ingesta. Kidneys normal. Bladder filled with urine. The brain was somewhat congested, but otherwise normal. Some sections of the brain were made but no lesions found. Cultures were made from the blood of the lungs and liver. From those obtained from the lung the culture was mixed. Those from the liver gave a pure culture which in all characteristics corresponded with those found in the abscesses previously examined.

The case had been diagnosed as toxemia, which appears to have been correct, and from the post-mortem cultures it would seem that there was a general infection and a condition of anemia as shown by the blood count. It was just such a case as would indicate a nuclein treatment and, although it ended fatally, there are a few points which would go to show that the nuclein was of considerable value. On the first day that the drug was administered there was an increase of over three thousand white cells or 73.77%, an increase which should be of great benefit in ridding the system of micro-organisms. The total increase between October 30th, when the dog entered the clinic, and December 20th, which was three days before the animal went home, was 7,600 leucocytes, (Oct. 30, 4,900—Dec. 20, 12,500), or in other words the resistance of the animal to infection had been more than doubled and I think it quite possible that if the animal had remained in the clinic it would have recovered. The rapid increase in flesh as seen on being returned January 9th would give rise to the suspicion that the animal had been immediately put on rich food, thereby clogging the channels of elimination and producing such a condition as would greatly favor the reproduction of toxemia.

It might be argued that the other treatment had something to do with the increase of leucocytes and this is quite possible. It must not be overlooked, however, that nuclein gave a rapid increase of leucocytes when first used and a gradual increase

during the entire time the case was under observation, and that it was the only agent which was given uninterruptedly during the entire period.

Case II.

This was an experimental case. The animal selected was a small dog of mixed breed, weight about thirty pounds. It was in good condition and in every way appeared to be normal. When the dog was wanted for examination, he was taken from the kennel into the research laboratory, a distance of about two hundred feet.

Date.	Time.	Respiration.	Pulse.	Temp.	Erythrocytes.	Leucocytes.	Hemog.
Oct. 24,	4:00 p. m.	..	...	....	5,008,000	11,440	85%
" 25,	10:00 a. m.	..	120	102.5	4,800,000	9,000	80%
" 28,	4:00 p. m.	..	120	102 5	4,900,000	12,333	....
Feb. 13,	9:30 a. m.	20	120	102.6	4,900,000	.....	....
	Gave one dram nuclein at 10:00 a. m. (hypodermic).						
Feb. 13,	10:15 a. m.	25	132	101.9	....	.....	...
	11:00 a. m.	..	...	102.2	....	.....	....
	1:00 p. m.	..	...	102.3	....	.....	....
Feb. 17,	8:30 a. m.	24	120	102.9	....	11,111	....
	Injected 40 minims of nuclein at 10:00 a. m.						
	10:15 a. m.	24	135	102	....	.....	....
	10:45 a. m.	..	...	102.2	....	14,058	....
	11:40 a. m.	..	...	102.5	....	.....	....
	1:00 p. m.	..	...	102.6	....	.....	....
Feb. 20,	9:30 a. m.	24	120	102.8	....	13,844	100%
	Injected thirty-five minims nuclein at 10:30 a. m.						
	10:45 a. m.	30	140	102.1	....	16,222 (11 a.m.)	
	11:15 a. m.	36	140	102.4	....	.....	....
	11:45 a. m.	26	140	102	....	.....	....
	1:00 p. m.	..	...	102	....	.....	....
Feb. 24.	In the preceding tests the initial temperature had been taken in the laboratory. I now began taking it in the kennel so that the exercise of the dog might not be the cause of an error.						
	8:45 a. m.	22	124	102	... .	.....	....
	9:00 a. m.	Taken in laboratory.					
		24	125	102.9	....	.....	....
	9:30 a. m.	24	124	102	....	.....	....
Feb. 27,	9:30 a. m.	..	(in kennel)	102	....	....	....
	9:45 a. m.	19	(in labor'y)	102 6	....	12,550	100%
	10:00 a. m.	48	130	102.7	....	.....	....
	10:25 a. m.	Gave twenty minims of nuclein (hypodermic).					

Date.	Time.	Respiration.	Pulse.	Temp.	Erythrocytes.	Leucocytes.	Hemog.
Feb. 27,	11:30 a. m.	..	...	...	....	16,666	....
	12:00 m.	40	130	102.3	....	15,333	....
Mar. 12,	9:30 a. m.	..	120	101.8	....	11,333	....
	Gave ten minims of nuclein at 10:00 a. m.						
	10:00 a. m.	..	120	101.8	....	.....	....
	10:45 a. m.	..	...	....	....	13,300	....
	11:15 a. m.	..	...	....	....	13,000	....
Mar. 17,	8:00 a. m.	..	120	102	... .	.....	....
	8:15 a. m.	..	...	....	....	13,111	100%
	8:20 a. m.	Injected twenty minims of nuclein.					
	9:45 a. m.	..	115	102	....	14,100	....
	10:00 a. m.	Injected forty minims more of nuclein.					
	10:30 a. m.	..	...	....	....	15,205	....

Case No. III.

Experimental dog, mixed breed, weight about eighteen pounds.

Date.	Time.	Respiration.	Pulse.	Temp.	Erythrocytes.	Leucocytes.	Hemog.
Mar. 5,	9:00 a. m.	..	140	104.8	......	11,222	100%
	9:30 a. m.	Gave thirty minims of nuclein.					
	9:30 a. m.	..	...	102.2	... .	.....	....
	10:30 a. m.	..	...	....	6,300,000	15,333	....
	11:30 a. m.	..	...	....	....	13,200	....
Mar. 6,	9:15 a. m.	..	...	101.6	....	.....	....
	9:45 a. m.	..	...	....	....	9,222	100%
	10:15 a. m.	Injected twenty minims of nuclein.					
	10:30 a. m.	..	...	102.2	....	9,000	....
	10:50 a. m.	..	...	....	....	8,000	....
	11:30 a. m.	..	...	....	....	9,000	...
Mar. 10,	8:00 a. m.	..	...	101.6	... .	8,333	....
	Injected twenty minims of nuclein at 9:00 a. m.						
	9:30 a. m.	..	...	....	....	8,330	....

In case No. 2 every experiment gave a rapid leucocytosis after the injection of nuclein. The highest being that of February 27, where there was an approximate increase of 4,000 white cells in about an hour. The respiration and pulse did not show any variation that could be considered due to the drug. In the earlier experiments it appeared that there was a fall in temperature of about one degree after the injection of the nuclein. But on taking the initial temperature in the kennel it was found

that the animal's temperature rose about one degree in transferring him to the laboratory and the apparent fall was probably only the return to normal when he again became quiet. The red cells or hemoglobin did not appear to offer any variation from the normal.

Case No. 3 did not give conclusive results in any direction. It would be well perhaps to state that this animal was very timid and so frightened when injected or otherwise experimented upon that it is quite possible that the virtue of the agent was more than overbalanced by the dog's mental condition.

In the Clinic of 1905, a case of mange was brought in for treatment. Along with the external treatment, nuclein was administered internally. The outcome was a complete and rapid recovery. Considering the severity of the case when it entered and contrasting it with similar cases we feel that no little credit was due to the nuclein treatment.

The Germicidal Properties of Nuclein.

For this I took a twenty-four hour culture of micrococcus pyogenes aureus, and from this inoculated two cubic centimeters of nuclein with one loopful of the organism. I then took six tubes of boullion and inoculated them with one loopful of the nuclein culture in the following order.

First tube	inoculated	at the	end of	1	minute.
Second tube	"	"	"	3	"
Third tube	"	"	"	5	"
Fourth tube	"	"	"	10	"
Fifth tube	"	"	"	20	"
Sixth tube	"	"	"	30	"

Examined after twenty-four hours and found no growth in any of the tubes.

In the next experiment 2 cc. of nuclein were diluted with an equal amount of sterile water. This was then inoculated with two loopfuls of the culture. Again six tubes of boullion were used, this time transferring two loopfuls of the nuclein culture into the boullion.

Tubes.	Time of inoculation.	24 hours later.
No. 1.	End of 1 minute.	Growth.
No. 2.	" 3 "	"
No. 3.	" 5 "	"
No. 4.	" 10 "	No growth.
No. 5.	" 15 "	" "
No. 6.	" 20 "	" "

This shows there is quite a marked germicidal action. It must be taken into account, however, that in the preparations used* the nuclein contains a small amount of trikresol as a preservative.

Following this a few experiments were conducted with a view to determine if nuclein was converted into peptones when taken into the digestive tract. It would appear that if nucleins were changed into peptones by the digestive ferments, they would be of no more value as therapeutic agents than peptones derived from other sources.

The following solutions were made:

Solution Pepsin { Pepsin, .3 gram.
.2% HCl 100 cc.

Solution Pancreatin { Pancreatin, 1 gram.
1% Sodium Carbonate, 40 cc.

Prepared four test tubes.

Tube 1. Pepsin solution 20 cc., Nuclein 5 cc.
Tube 2. Pancreatin solution 15 cc., Nuclein 2 cc.
Tube 3. Pepsin solution 25 cc., Nuclein tablets (three).
Tube 4. Pancreatin solution 20 cc., Nuclein tablets (three).

These were put in an incubator at 40° C for one hour and a half, after which they were tested for peptones by adding an excess of 20% caustic potash solution and a drop or two of a solution of copper sulphate. This test gives a pink color with peptones, but albumose gives the same reaction. To determine if the latter is present some of the solution was saturated with ammonium sulphate, filtered and tested. This serves to precipitate and remove the albumose, and if the filtrate gives a pink color we have peptones. Tests were made for syntonin and alkali albumin by the contact method. 1% sodium carbonate solution being used for the former and .2% HCl for the latter. An affirmative test is shown in either case by a white precipitate at the neutral zone.

*Parke Davis.

No. Tube.	Peptones.	Albumose.	Syntonin.	Alk. Albumin.
1	None	Present	None	None
2	None	Present	None	Present
3	None	Present	None	None
4	None	Present	None	Present

The tubes were returned to the incubator for forty-eight hours, but when re-examined showed the same results.

As a check to this test I prepared some more of the same digestive solutions and put them in the incubator for one hour—no nuclein being added. At the end of this time both solutions gave the pink color indicating peptones or albumose. The tubes were then returned to the incubator for twenty-four hours. When tested both were found to contain albumose but no peptone.

This concludes my experiments with nuclein and, although the work done is not conclusive in any particular, it would indicate that :

1st. Nuclein does cause a rapid leucocytosis, a single dose being sufficient to increase these cells several thousand per cubic millimeter of blood.

2nd. The red cells are affected only to a slight degree.

3rd. It is non-toxic. Dram doses given hypodermically do not effect pulse, respiration or temperature in the normal animal.

4th. It does possess germicidal properties to a considerable extent.

5th. It is not converted into peptones by the digestive ferments.

In conclusion I desire to acknowledge my indebtedness to Ward Giltner for assistance freely given in many of the blood counts, and to Dr. Fish for suggestions and use of drugs from the Department of Physiology and Pharmacology.

REFERENCES :

HARE—*Practical Therapeutics, 5th edition.*
POTTER—*Materia Medica, Pharmacy and Therapeutics.*
United States Dispensatory, 18th edition.
BUTLER—*Materia Medica, Therapeutics and Pharmacology.*
PARKE, DAVIS & CO.—*Nuclein, its Origin, Nature and Therapeutics.*
METCHNIKOFF—*Immunity in Infective Diseases.*

ARECOLINE HYDROBROMIDE.

PIERRE A. FISH.

Arecoline is the alkaloid obtained from the Betel or Areca nut. Pure arecoline is a colorless oily fluid, miscible with water, alcohol, chloroform and ether. It is present in the areca nut to the extent of about 0.1%. The alkaloid is very toxic and forms crystalline salts; the principal one of which is arecoline hydrobromide, $C_8H_{13}NO_2BrH$. Two other alkaloids have been described, one under the name arecaine and the other, existing in traces, as guvacine.

The investigations of Marmé and Fröhner point out many resemblances between the effects of arecoline and the combined effects of eserine and pilocarpine. It likewise resembles muscarine in its action.

E. Fröhner has noted the following actions of arecoline upon the horse: It is a strong sialagogue. Doses of $\frac{1}{6}$ to $\frac{5}{6}$ grain (0.01—0.05) cause the saliva to flow in about five minutes, reaching the maximum in one-half hour and continuing to flow for about an hour. It produces tetanic contractions of the intestinal muscles and excites the intestinal glands. Horses purge, on the average, from doses of $\frac{5}{6}$ to $1\frac{1}{2}$ grains (0.05—0.1), the first discharge appearing in from one-fourth to one-half hour after the injection. Purgation is usually accompanied by light colicy symptoms. Large doses of arecoline excite the sweat glands and cause increased perspiration. There have also been observed nasal discharge (from stimulation of the glands of the nasal mucosa) and urination. The local application of a solution of arecoline (0.1—1%) to the eyeball causes marked contraction of the pupil, lasting for several hours. Subcutaneous injections, however, do not produce this effect. Arecoline has a marked anthelmintic action. Cardiac action is slowed (vagus stimulation). Toxic doses produce arhythmia of the heart; fall in blood pressure and temperature as well as a marked acceleration

of the pulse (paralysis of the vagus). Large doses are fatal because of respiratory paralysis with tetanic contractions. Doses of $3\frac{3}{4}$ grains (0.25) are toxic for the horse; $7\frac{1}{2}$ grains (0.5) are fatal.

Bocquillon-Limousin gives as the fatal doses: for the rabbit $\frac{1}{3}$ to $\frac{5}{6}$ grain (0.025—0.050); for the cat $\frac{1}{3}$ grain (0.020); for the dog $1\frac{1}{6}$ grains (0.075). H. J. Milks, in some experiments at the New York State Veterinary College, using Merck's preparation of arecoline hydrobromide, found that after previous injections of small doses that the fatal dose must thereby apparently be increased. A dog, weighing about 25 lbs., received subcutaneously on four successive days doses of $\frac{1}{20}$, $\frac{1}{5}$, $\frac{1}{10}$ and 1 grain. The dog was apparently as well as ever the day following the injection of the 1 grain. Three days later 2 grains were injected and were followed by toxic symptoms with blood passing in the feces. After six days the dog apparently recovered. Two weeks from the beginning of the experiment 3 grains were injected during the afternoon and the dog died the following forenoon. During the post mortem, several tape worms (seven) were found in the small intestine, indicating that there was no vermifuge effect from the injections, as no segments of the worms were observed to have passed in the feces. In another dog, where some of the arecoline solution was injected into a segment of the intestine, living tape worms were found after having been in contact with the solution for several minutes. In kittens weighing from $\frac{3}{4}$ to $2\frac{1}{2}$ lbs., $\frac{1}{8}$ grain was fatal. In a cat weighing $4\frac{1}{4}$ lbs., $\frac{1}{4}$ grain was fatal. In general the heart continued to beat for a time after respiration had ceased.

Dr. H. E. Titus of Ames, Iowa, experimented with arecoline hydrobromate upon fourteen cases, including horses, cows, dogs and one sheep. The sheep was in an emaciated condition and died shortly after a dose of 5 milligrams ($\frac{1}{12}$ grain). One of the cows suffering from parturient apoplexy, died after receiving two doses of 50 milligrams ($\frac{5}{6}$ grain) each. He used the drug successfully in cases of colic and laminitis in horses.

From a therapeutic standpoint, the drug has proven of considerable value in the treatment of colic and laminitis. It has also been recommended in azoturia combined with sedatives;

also where myotics are indicated. Fröhner states that, like pilocarpine, arecoline is a good resorbent for internal and external transudates, especially in cerebral dropsy and phlegmon, and that several cases of blind staggers have been benefitted.

The effect of arecoline hydrobromide upon the circulatory system is pronounced. The writer has taken blood pressure tracings from five horses under chloroform anesthesia, following the intravenous and hypodermic injection of the drug and the results are briefly summarized as follows:

Horse No. 30 was badly affected with the heaves. Weight 910 lbs. (413 kilograms). The normal blood pressure was found to measure 116 mm. of Hg. Twenty and six-tenths cc. of a 0.2% solution of arecoline hydrobromide, the equivalent of 0.1 mg. per Kg. or a total of about $\frac{2}{3}$ grain, were injected into the right jugular vein. The effects were almost immediate. There was profuse salivation; slowing of the heart, with some irregularity in its beat and a fall in blood pressure to 62 mm. (Fig. 1). The pupils became dilated and the blood was very dark indicating an excessive amount of CO_2. The horse showed toxic symptoms and the same amount of atropine sulphate was injected into the jugular as an antidote. Improvement resulted as shown by the more rapid beat of the heart and an increase of blood pressure to 108 mm. and later to 130 mm. No more atropine was given and the horse died later, something within two hours after the experiment.

Horse No. 31. Weight 1084 lbs. (492 kilograms). 12.3 cc. of a 0.2% solution of arecoline were injected (0.05 mg. per Kg.) or a total of about $\frac{1}{3}$ grain. The blood pressure ranged from 98 to 84 mm. before, but after the injection soon fell to 66 mm. The amplitude of the beat was more than doubled with the corresponding slowing of the beat. A moderate electrical stimulus applied to the vagus produced but slight effect. In this case the drug also produced very pronounced effects. Marked salivation soon occurred and profuse sweating around the anus and flanks. The nasal mucosa became cyanotic and this condition persisted after the use of the antidote. The condition of the horse became quite serious as to breathing and a tracheotomy tube was introduced into the trachea with benefit. It is doubtful if the horse

would have survived without the use of the tube. One and one-third grains of atropine sulphate (four times the dose of the arecoline) was injected into the jugular. The beat of the heart soon increased in frequency and the blood pressure rose to 114 mm.

No. 32 was a mare weighing 790 lbs. (359 kilograms). She had been spayed just previous to the experiment. One grain of the arecoline hydrobromide (0.19 mg. per Kg.) was injected *sub cutem.* The effect was slower than when used intravenously and the first indication of its action was a lowering of the blood pressure, which fell from a normal of 158 mm. to 134 mm. Then quite suddenly the heart became irregular and slow with the amplitude of the beat much diminished. The blood pressure fell to 78 mm. and the heart stopped for a short time apparently in systole. The vapor of ammonia was inhaled and this was soon followed by improvement in the character of the beat and a rise in blood pressure to 98 mm. (Fig. 2). There was little or no salivation in this case, but the pupils were dilated and the oral mucosa was somewhat cyanotic indicating an increased amount of CO_2 in the blood. Later one-half grain of atropine sulphate was injected intravenously with benefit.

No. 49. Mare weighing 815 lbs. (370.5 Kg.). Spayed shortly before the experiment. Thirty-seven-sixty-fourths of a grain of arecoline hydrobromide (0.1 mg. per Kg.) was injected into the jugular. The blood pressure fell quite rapidly from 164 mm. to 102 mm., and a little later to 90 mm., with a considerable increase in the amplitude of the beat or slowing of the heart. An injection of $\frac{55}{64}$ grain of atropine sulphate (0.15 mg. per Kg.) caused a rapid rise in blood pressure with a decreased amplitude or quickening of the beat. The blood pressure finally rose to 190 mm.

No. 55 was also a mare, spayed just before the experiment. She weighed 910 lbs. (414 Kg.). In the same dose, there was administered one-half grain of arecoline hydrobromide and one-half grain of atropine sulphate intravenously (0.077 mg. of each per Kg.). The arecoline effect was produced first as shown by a slowing and slight irregularity of the heart, with a fall in blood pressure from 114 mm. to 68 mm. Then quite suddenly the atropine effect appeared, as shown by the quickened heart beat and

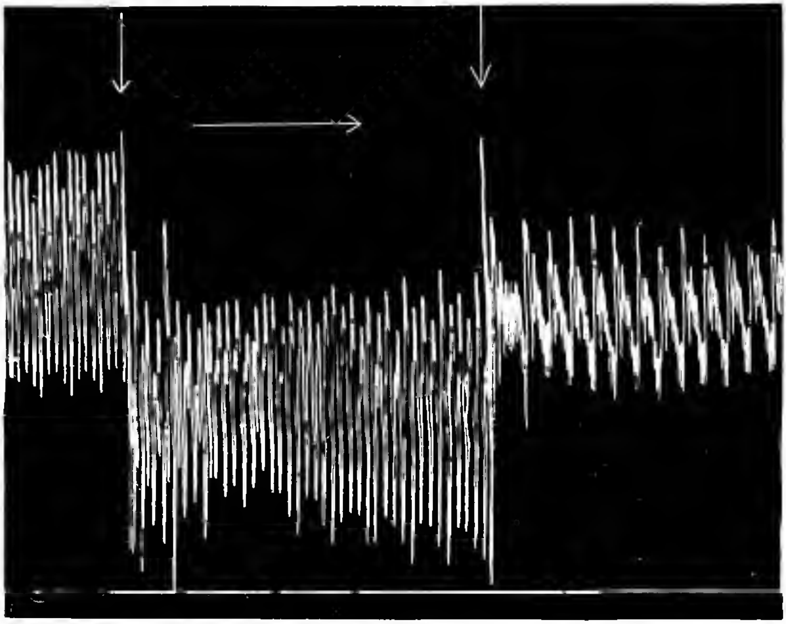


FIG. 1.

Horse No. 30. The short tracing to the left is the normal. The left vertical arrow shows when the arecoline was injected. Note the fall in blood pressure. The second vertical arrow shows when the atropine sulphate was injected followed by a rise in blood pressure and more rapid heart beat.

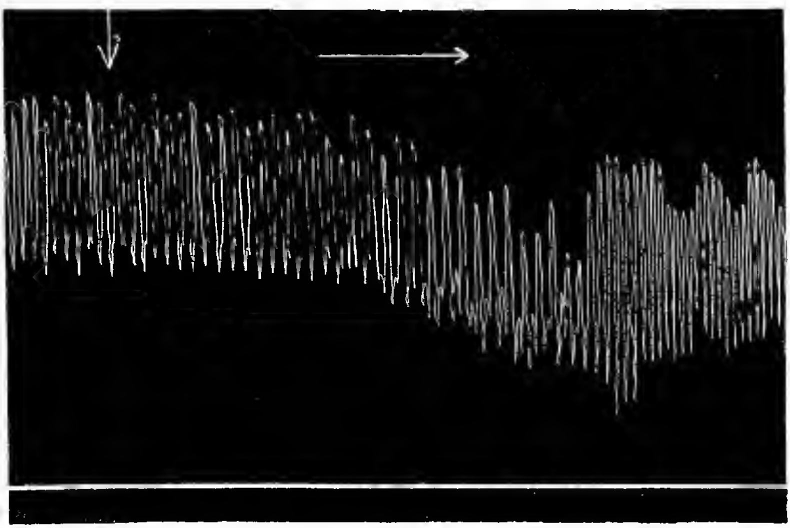


FIG. 3.

Horse No. 55. The vertical arrow indicates when the combined arecoline and atropine were injected into the jugular. Note the slowing of the heart beat and fall in pressure—the arecoline effect. Later the pressure rises and the heart beats faster under the influence of the atropine.

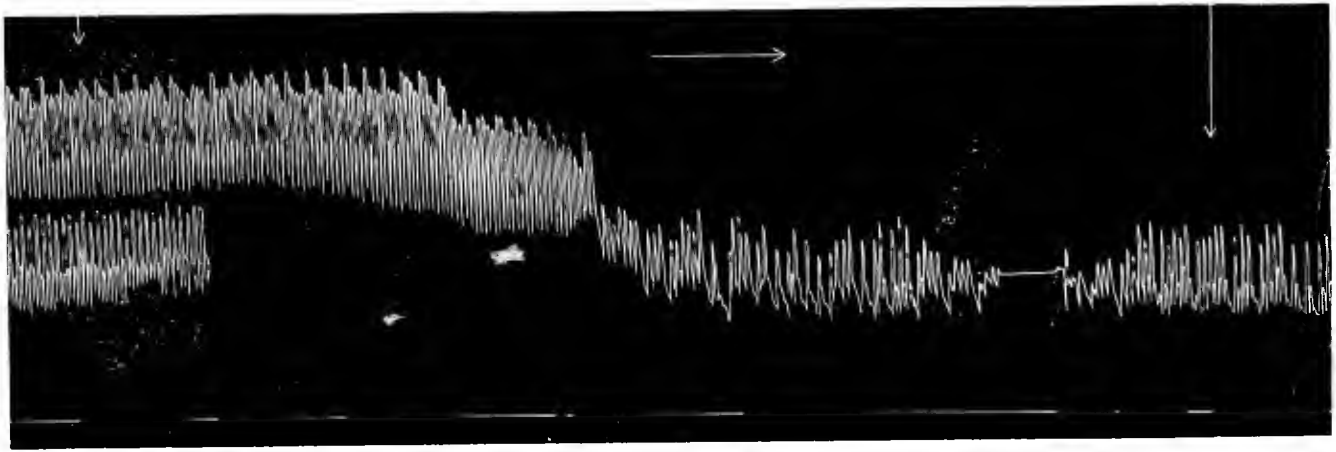


FIG 2.

Horse No. 32. Blood pressure tracing after injection of 1 grain of arecoline hydrobromide subcutaneously. The short vertical arrow at the left indicates when the injection was made. The longer arrow at the right shows when the ammonia vapor was inhaled. The lower tracing at the left shows the improved conditions of the heart beat after the ammonia.

a rise in the blood pressure to 88 mm. (Fig. 3). The blood pressure gradually fell again to 68 mm. and the amplitude of the beat increased, but the heart did not beat as slowly as before the injection.

In all five cases there was a uniformity in lowering blood pressure and increasing the amplitude or slowing of the heart beat. In numbers 30, 31 and 49, the atropine caused the blood pressure to rise a point higher than normal and in all cases accelerated the action of the heart. In No. 32 no tracing was taken after the injection of the atropine. In No. 55, with the simultaneous injection of equal amounts of arecoline and atropine, the arecoline effects were apparently the stronger in that there was slowing and irregularity of the heart, with a fall in blood pressure. The atropine seemed to successfully counteract the irregularity and to a large extent the slowing of the heart, but the blood pressure gradually fell to that caused by the arecoline. A larger amount of atropine or repeated doses of it might have counteracted the arecoline more completely. As an antidote to arecoline, atropine seems to be quite successful.

In routine practice, as in colic, etc., the atropine may be used in small dosage in combination with or following the arecoline to guard the circulation and respiration against the depressing effects of the latter.

BARIUM CHLORIDE IN NUX POISONING.

H. B. TILLOU AND L. S. BACKUS.

The subject was a horse about fifteen years old, weighing about 1000 lbs. Was lame in the near fore leg, caused by badly contracted flexor tendons.

As an experiment, February 14, 1907, we gave four drams of powdered Nux Vomica at 1:30 P. M. One hour later he began to show symptoms of poisoning, as evidenced by restlessness, colicy pains, hurried, difficult breathing, muscular spasms, excessive perspiration. Pulse 120, temperature 102. In one of the spasms he fell to the floor and was unable to rise.

As an antidote he was given 20 cc. of Lugol's solution in a pint of water, and three ounces of chloroform by inhalation. At 3:35 the horse was showing no signs of improvement. The pulse was 104 and the respirations 54. He was then given 15 grains of barium chloride hypodermically. At 3:43 P. M. the pulse was reduced to 84, was more regular and strong. At 3:50 P. M. the pulse was 72. At 3:57 P. M. the pulse was 60. The respirations at 3:50 P. M. had been reduced to 42 and were deeper and not so labored. At 4:30 P. M. the animal was much improved and got upon his feet. At 5:00 P. M. the pulse was 50, regular and full; the respirations were 28 and normal. The animal began to eat and appeared to be in no pain. After the injection of the barium chloride there were three evacuations of the bowels.

February 16, 1907, noon. The same amount (4 drams of Nux Vomica) was again given to the horse. At 1:30 P. M. he began to show symptoms of poisoning, as in the preceding experiment. The pulse was 60 and the respirations were 72 per minute.

At 2:30 P. M. he was given 15 grains of barium chloride intravenously. At 2:45 P. M., or fifteen minutes after the medicine was given, the muscles began to relax and the spasms began

to cease. At 2:50 P. M., or 20 minutes after injection, the animal ceased sweating.

At 2:40 P. M. the respirations were reduced to 60 per minute, and not so labored. At 3:00 P. M. the pulse was sixty ; respirations 25 and normal. The spasms had entirely disappeared. The general appearance was much improved. The patient drank a pail of water and began to eat hay. At 3:45 P. M. the pulse was 55 and the respirations 23. In this experiment the barium chloride produced five evacuations of the bowels.

GLANDERS AND BOVINE SERUM.

C. L. ROADHOUSE AND LEIGH GILTNER.

Important work in connection with the serum therapy of glanders has been carried on by Helman, Semmer and Itzkovitch, Pilalvios, Bonome and Vivaldi, Johne, Schindelka, Prieus and Babes. Since bovine animals are immune to the ravages of glanders, it was believed that an immune body or antitoxin might be found in the blood serum which, when injected into an affected animal, might neutralize the toxin produced by the invading organism and aid in bringing about recovery.

The work of Babes, extracts of which appear in the Recueil de Medicine for 1893, and the Comptes rendus de l'academie des Sciences, 12 Decembre 1892, was somewhat similar to that which we had planned and a brief reference to his method and results are herewith given. Babes used what he called an extract of beef's blood. It was prepared by collecting the blood of the ox in sterile flasks and keeping it at a low temperature for several hours. Water and powdered zinc were added and the mixture shaken. The zinc was used to precipitate the solid particles of the blood, including bacteria and serum albumin. The mixture was filtered and a clear fluid obtained, to which was added potassium *sulphuret* in order to remove any traces of dissolved zinc. The mixture was concentrated to a residue in a vacuum at 35° C. and the residue dissolved in a mixture of equal parts of water and sterilized glycerine. This extract Babes used in his experiments.

Babes injected this extract into glandered and non-glandered horses and guinea pigs. The glandered animals gave a thermal reaction similar to that produced by Mallein. There was no reaction in the non-glandered animals. Babes states: " In my recent experiments I am led to foresee that the beef's serum possesses a specific therapeutic and vaccinal action in glanders."

Our own method differed from that of Babes in that the beef's blood received no special treatment further than to collect it in sterile flasks, allow the serum to separate from the clot, remove it and keep it in as aseptic a condition as possible. Babes apparently made his extract from the blood as a whole, while in our work the serum only was used.

The question of any hemolytic action of the beef serum was considered early in the work, as this condition would naturally have an important bearing from a therapeutic standpoint on the continued injection of the serum. The following statements from Nuttall are interesting in this connection: 1. The transfusion of foreign bloods to man led to the formation of clots, thrombi, serous exudates and hemolysis. 2. Hemolysins act by separating the hemoglobin from the stroma of the blood corpuscle, causing the blood with which they come in contact, to lake. (The hemoglobin is found in the urine). 3. The hemolytic action of the serum is the dissolution of the cell. 4. In 1898, Grey treated rabbits with increasing doses of eel serum and they gradually developed increasing quantities of antitoxin. Eel serum as a type of hemolytic serum is destructive to red corpuscles, leucocytes, renal epithelium and nerve cells. 5 Ox serum was found to be injurious to man in the transfusion experiments of Landois, because it hemolysed human corpuscles. Friedenthal found it to hemolyse the corpuscles of the pig, horse, rabbit, dog, cat and also man. When injected into guinea pigs, it produced infiltration and necrosis.

Two guinea pigs were experimented upon with the bovine serum. Pig No. 1 received subcutaneous injections of the serum from November 22 to December 14, 1905, getting a total of 19½ cc. There was no abnormal change in temperature during this period. The post-mortem showed an edematous sloughing and hemorrhagic condition of the subcutaneous connective tissue at the point of injection.

In guinea pig No. 2 the bovine serum was injected intraperitoneally. Three cubic centimeters of the serum were injected February 6th. The temperature of February 5th was 99.4°. From the 6th to the 9th inclusive it was 98.9°. On the 10th, 3 cc. of the serum were again injected. The temperature on the 10th

and 11th was 99.4°. On the 12th the guinea pig died. The post-mortem showed local inflammation and thickening in the vicinity of the puncture; also congestion of the liver.

According to Uhlenhuth, Rommo, Weiss and Guinard, the lethal dose of ox serum intravenously for the rabbit is 6 cc. to 9 cc. per kilogram of weight. In the above experiment a total of 6 cc. was fatal to the guinea pig.

EXPERIMENTS UPON HORSES. Horse No. 1 was in good condition, aged about thirty years, and weighed 901 lbs. During the first period, from November 22nd to December 21st, 1905, sixteen injections of the ox serum were made *subcutaneously*. The single doses ranged from 10 cc. to 20 cc. and a total of 265 cc. of the serum was injected during this period. The temperature was taken daily at first and then at intervals. It remained normal, ranging from 98.6° to 99.6°. On December 22nd, a microscopic smear was made and stained by Jenner's method, but nothing abnormal was noticed. In all of the subcutaneous injections of the serum, there was a marked circumscribed swelling with considerable soreness at the point of injection, which lasted about two days.

From December 22nd to February 22nd the horse received the serum intravenously. At first he received 5 cc., then 10 cc. and finally 20 cc. of the serum at a dose. The total amount injected intravenously for this period was 565 cc. The horse was weighed on January 5th and was found to have lost 70 pounds.

An examination of the blood gave the following results:

	Horse No. 1.	Normal.
Hemoglobin	65%	94%
Erythrocytes	5,000,000	7,900,000
Leucocytes	8,000	5,000 to 10,000
Hb. Index	70%	100%

The urine was also examined and gave the following:

	Horse No. 1.	Normal.
Specific gravity	1050	1025 to 1050
Reaction	alkaline	alkaline
Chlorides	7.7 per 1000	8 to 14 per 1000
Sulphates	.35 per 1000	2 to 3 per 1000
Urea	32. per 1000	20 to 40 per 1000

A spectroscopic examination showed the absence of hemoglobin, so that, on the whole, the urine appeared to be in a fairly normal condition.

On February 22nd, 1906, horse No. 2 was procured as a check animal. He was in fair condition and quite spirited, although about twenty years old.

Both animals were tested for glanders by the agglutination method and were found to be free from the disease. Both horses were then inoculated subcutaneously with 3½ cc. of a virulent culture of Bacterium Mallei. A circumscribed swelling with tenderness was produced in each animal.

Before the injection, the temperature of horse No. 1 was 99.2° and that of No. 2, 99.6°. After the injection, the temperature of horse No. 1 went up to 100.6°, then fell to 100.3° and remained there for a week. In horse No. 2, the temperature remained at 99.6° and 99.5° until March 4th, when death occurred.

The post-mortem of horse No. 2 showed a local hemorrhagic and edematous condition of the subcutaneous connective tissue and paniculus over an area covering about 4″ x 12″ in the vicinity of the seat of inoculation. A similar condition existed beneath the scapula and posteriorly across the chest wall to the sternum. The agglutination test on the post-mortem blood gave the reaction for glanders.

Aside from the local swelling and a slight rise in temperature, horse No. 1 developed no symptoms of glanders. The agglutinatian test gave no reaction for glanders.

On April 2nd, horse No. 1 again received intravenous injections of the serum. Larger doses, ranging from 35 cc. to 65 cc. were given, and during the eight days from April 2nd to 9th, inclusive, a total of 420 cc. of the serum was injected.

On April 14th, horse No. 3 was procured as another check animal. He was a large draft animal, about eight years of age, strong and in good condition aside from being affected with paraplegia which, however, did not interfere with his value for the experiment. The agglutination test showed that he was free from glanders.

Horses 1 and 3 were inoculated subcutaneously with 10 cc. of a culture of Bacterium Mallei, which had been grown at 40° C.

for three days, probably producing some degree of attenuation. This inoculation produced only slight swelling, which disappeared after one day. As there were no apparent symptoms from the above inoculation, it was repeated on April 20th, with 10 cc. of a virulent culture of Bacterium Mallei. The following table shows the temperatures of each horse for five days:

	Horse No. 1.	Horse No. 3.
April 20	98.6 degrees	98.5 degrees
April 21	102.3 "	101.1 "
April 22	104.5 "	101.4 "
April 23	105.5 "	102.5 "
April 24		96. "

On April 21, horse No. 3 showed a marked local swelling, with pain at the point of inoculation. On the 22nd there was increased swelling and pain. The horse was in a weak condition. On the 23d there was loss of appetite and greater weakness. On the 24th the horse was down in the stall and died at noon. Blood was drawn from the jugular vein and the serum collected. This was submitted to the agglutination test and a positive reaction obtained which showed the horse to have been glandered.

Post-mortem, Horse No. 3. At the point of inoculation there was a hemorrhagic area containing serous exudate and extending from the top of the neck to the scapulo-humeral articulation. There was a thickened and hardened condition at the point of inoculation over an area 4″ x 6″, containing purulent matter. The lungs were filled throughout with miliary nodules. The mediastinal lymph glands were enlarged, hemorrhagic and dark colored. There was a hemorrhagic and edematous condition of the tissue around the trachea and aorta. The splenic pulp was soft.

On April 26th, a male giunea pig was inoculated subcutaneously with nodules from the lung. The guinea pig died May 21st, with orchitis and abscess of the inguinal lymph gland on the same side as the point of inoculation. Pure culture organisms were obtained from the testicle.

Horse No. 1 had received no serum for two weeks previous to the inoculation of 10 cc. of the virulent culture on April 20th. On April 24th, fifty cubic centimeters of the serum were injected. Immediately following this injection, the horse showed a marked

increase in the number of respirations; the breathing became labored but returned to normal within a few minutes. The reaction from the above injection is given below:

April 24.	4:00 P. M.	Temperature	104.0	degrees.
	4:30 P. M.	"	103.8	"
	6:00 P. M.	"	104.0	"
	12:00 P. M.	"	104.7	"
April 25.	2:00 A. M.	"	105.4	"
	4:30 A. M.	"	105.2	"
	6:00 A. M.	"	105.3	"
	8:00 A. M.	"	105.3	"
	11:00 A. M.	"	104.7	"
	4:00 P. M.	"	105.1	"

At 4:00 P. M. 40 cc. of the serum were injected and the symptoms of April 24th were not noticed.

On April 26th, the temperature at 10:00 A. M. was 103.7°; at 4:30 it was 105°. At this time 50 cc. of the serum were injected. On April 27th, the temperature was 104.5°. The abscess which had formed at the point of inoculation was opened, the pus evacuated, and the area disinfected with strong lysol solution. On April 28th, the temperature was 103.8°. Fifty cubic centimeters of the serum were injected. There was slight dyspnoea as on April 24. There was a slight serous nasal discharge. On April 29th, the temperature was 103.8°. There was swelling of the nostril, labored breathing and thick mucous discharge. On April 30th, the temperature was 102.5°. There was more pronounced thickening of the nostril; thick, blood-stained mucous discharge from the nose. The breathing was so labored and the symptoms of suffocation so impending, that tracheotomy was performed. Seventy cubic centimeters of the serum were injected. Blood was drawn from the jugular vein and the serum collected, which by the agglutination test showed the animal to have been glandered.

Post-mortem Horse No. 1. There was an edematous condition of the connective tissue under the skin above the false nostril and in all the surrounding tissues. The mucous membrane of the nasal septum was dark red in color, infiltrated and showed marked pea-like yellowish elevations with red areolæ. On the

floor of the nasal fossa and septum nasi, the mucosa of the facial sinuses was necrotic, and in places the necrosis extended into the bone. The sinuses contained a thick, viscid liquid. There was a thickened condition of the mucosa of the turbinated bones. The spleen was enlarged to three times its normal size and the pulp was soft and dark colored. The kidneys and the liver were enlarged and friable. There was a hemorrhagic and enlarged condition of the anterior mediastinal lymph glands.

Summary.

Aside from some anemia and a reduced number of red corpuscles as shown in the blood count, there were no marked or apparent injurious hemolytic effects from the injection of the bovine serum.

The evidence is much less complete than might be desired with regard to the effects of the serum upon glanders. Such as it is it seems to be favorable to the belief that the serum imparts some power of resistance to the virus and that it has some value as a diagnostic agent.

In the first experiment the horse treated with the serum did not respond to the agglutination test for glanders; while the second horse did, although both were inoculated with the glanders virus at the same time and the agglutination tests were made coincidently at a suitable period after the inoculations.

In the second experiment both horses came down with glanders after an inoculation of an unusually large amount of virus. But the serum-treated horse survived for a week longer than the control. In the matter of temperature, the serum-treated horse showed a constantly higher temperature than the control after the virus had taken effect. Succeeding injections of the serum caused a still higher rise temporarily in the experimental horse.

HYDROCYANIC ACID IN CHLOROFORM NARCOSIS.

L. S. BACKUS.

This agent was brought to my attention for the above purpose while reading the work on "Surgical Diseases of the Dog and Cat," by Hobday. He says: "Hydrocyanic acid first suggested itself as an antidote to chloroform whilst watching the powerful respiratory efforts which it so rapidly causes, when given to produce toxic effects. It is of especial value because it not only stimulates the respiratory center to recommence if once it has ceased, but if given in full medicinal doses, it maintains the breathing until it is able to look after itself, and at the same time by the deep inspirations produced it causes the entrance of a large amount of air into the system. Its effects, too, on the heart are beneficial. The dose recommended of Scheele's strength, to be placed on the tongue averages about one-eighth of a minim for each pound of body weight."

In order to test the value of the above observations the following experiments were performed.

Exp. 1. Administered chloroform to a full grown cat until respiration ceased, then put two drops of dilute hydrocyanic acid on the back of the tongue and performed artificial respiration. Respirations began at once.

Exp. 2. Subject was a male dog, weight about forty pounds. While in chloroform anesthesia the respirations suddenly ceased. Five drops of hydrocyanic acid were put on the tongue and artificial respiration performed. The respiratory function was restored.

Exp. 3. Small kitten. Chloroform was administered until there was a cessation of the respirations. One minim of the acid was placed on the tongue and artificial respiration performed. The breathing was at once restored.

Exp. 4. Horse. Weighed about 1000 lbs. Completely anesthetized. Into the jugular was injected one dram of hydrocyanic acid. The respirations immediately became deeper and stronger. The pulse was strengthened. At the outset, It was planned to destroy the horse so ten minutes later two drams more of the acid were injected. This caused an almost instant cessation of heart beat and respiration.

SODIUM BENZOATE AND METABOLISM.

PIERRE A. FISH.

Complete experiments in metabolism were not attempted. The feces were not examined nor was any account taken of the perspiration or respiration. Careful examinations were made of the urine and changes in the system due to metabolic activity would, it is believed, cause corresponding changes in this excretion.

Experiments were tried upon two dogs and upon two men, the dogs being killed at the end of the experiment and certain of their tissues examined for any pathological changes.

As there were a great many urinary examinations to be made, the methods commonly used in clinical work were adopted and are believed to be sufficiently accurate for comparison. Because it is expeditious the centrifuge was used for the determination of the chlorides, phosphates and sulphates after first being checked by volumetric determinations, and the value of each 0.1 cc. of the precipitate in the centrifuge calculated on the basis of parts per thousand. Urea determinations were made with the Doremus ureometer, as modified by Hinds, in connection with the sodium hypobromite solution. For the uric acid test Ruhemann's Uricometer was employed.

Dog. No. 1. A black male dog of uncertain breed. Was apparently healthy at the time the experiment began, but had been troubled with a skin affection three months before. The dog was under observation for normal data from March 15th to 27th. During this interval the pulse ranged from 104 to 112 and the temperature from 102.2 to 102.8 F. March 20th the weight was 42 pounds. The diet consisted of Spratt's dog biscuits and plenty of water. On March 27th sodium benzoate was administered in tablet form to the extent of 120 grains (8 grams) a day. This amount was administered in three doses of 40 grains each. After the first day it was given in two doses of 60 grains each. Just before beginning the benzoate the dog was again

weighed and this time weighed 40.50 lbs. For the first three days, emesis occurred once or more daily, shortly after the administration of the benzoate. Later the emesis was not observed. The pulse and temperature were noted at occasional intervals and the former was found to range from 98 to 102 and the latter from 101.8 degrees to 102.6 degrees F. From March 31st to April 5th, inclusive, the sodium benzoate was given in solution, 60 grains of the powder being dissolved in 2 fluid ounces of water for each dose twice a day. This form of administration caused considerable coughing and some nausea but no emesis. Later the coughing was not so marked and sometimes was not present. The dog was killed April 6th and at his death weighed 41.25 lbs.

The urine for the 24 hours was collected and examined on alternate days. Microscopic examinations were made on each occasion and revealed a crystalline deposit. These crystals were soluble in acetic acid and were regarded as phosphates. On two occasions there was some effervescence indicating the presence of carbonates. Small masses of epithelial debris and dandruff scales were also encountered, probably having gotten into the urine, after it was passed, from the skin. The result of the chemical exrmination for the 24-hour urine is shown in the following table, the average being taken for the period when no benzoate was taken, followed by the average for the period when the benzoate was taken :

	Amt.	Sp. gr.	Solids.	Chlor.	Phosph.	Sulph.	Urea.	Uric ac.	Sug.	Alb.
Average of 4 exams. Normal Period.	310cc.	1036	26.422	4.168	1.206	1.736	16.87	0.1813	....	trace
Average of 4 exams. Benzoate Period.	371cc.	1045.5	38.825	4.175	2.163	3.147	18.93	0.234	0.8%	pres.
Maximum Normal Period.	400cc.	1042	37.280	7.396	1.995	3.60	24.00	0.261	....	....
Maximum Benzoate Period	450cc.	1050	45.015	7.766	2.591	5.850	21.60	0.342	....	....
Minimum Normal Period	220cc.	1026	13.327	1.695	0.840	0.825	7.48	0.132	....	....
Minimum Benzoate Period.	250cc.	1040	29.125	1.265	1.641	1.937	15.00	0.185	....	....

The fact that some albumin was found during the normal as well as during the benzoate period, although in greater amount during the latter, would indicate some departure from a true normal condition before the experiment was begun. The day following the administration of the benzoate showed the presence of albumin to the extent of 0.375 parts per thousand of urine. After this it fell to a mere trace. Although sugar is not reported as present during the normal period the tests were somewhat suspicious, as Fehling's solution became opaque, but not red, and bismuth was slightly darkened. Glycuronic acid, a constituent of the urine of the dog, has a reducing effect upon copper solutions, and it was believed that this substance might have simulated the sugar reaction. When, however, the benzoate was administered the tests became more pronounced, the Fehling's solution gave a red precipitate of cuprous oxide, the bismuth became black, and to make the result more conclusive in favor of sugar some of the urine caused fermentation with yeast in a fermentation tube. Whatever the substance, sodium benzoate increased its amount and caused decidedly stronger reactions with the reagents.

The effect of the benzoate upon the urine as a whole was to increase its amount and to cause a gain in all of the constituents. The constituent least affected was the chlorides; those most increased were the phosphates and sulphates, each of which was nearly doubled in quantity.

Dog No. 2. This dog was a female. Her ovaries had been removed a month or two previous to the beginning of the experiment. She was under observation from March 15th to May 17th. Her weight on March 20th was 41.5 lbs. Her pulse from March 15th to 17th (the normal period) ranged from 100 to 114. Her temperature ranged from 102 to 102.8 degrees F. Aside from an occasional irregularity in the heart beat, the dog seemed to be in excellent health. Her diet was the same as that provided for No. 1. Records of her pulse and temperature were kept through the benzoate period up to April 8th, then they were discontinued. During this period her pulse ranged from 104 to 116 and her temperature from 101.8 to 102.6 degrees F.

In this experiment, the idea was to study the effect of smaller doses administered for a longer period of time. With this exception the details of the experiment were practically the same as for Dog No. 1. According to changes in the dosage, the experiment may be divided into five periods: 1st, the normal or fore period, from March 15th to 17th. 2nd, the 4-gram period, during which 4 grams of benzoate of sodium were administered daily, (one-half the amount given to dog No. 1), from March 27th to April 17th. 3rd, the 6-gram period, from April 17th to April 23rd. 4th, the 2-gram period, from April 23rd to May 8th. 5th, the after period, when no benzoate was administered, from May 8th to May 17th.

Just before the administration of sodium benzoate March 27th the dog was found to weigh 40.5 lbs. The 4 grams (or 60 grains) of the benzoate were administered in three doses of 20 grains each. After the first day it was given in two doses of 30 grains (2 grams) each. Emesis also occurred in this dog but not quite as frequently as in No. 1. From March 31st to April 5th, inclusive, 30 grains of the powdered benzoate dissolved in water were administered twice daily. In this dog no coughing, nausea or emesis were observed while the drug was given in solution. The change from the tablet form to the powder in solution was made because the question arose as to whether the milk sugar which probably formed a part of the tablet had any influence upon the production of sugar in the urine. As the urinary results did not change with the change in the form of administering the benzoate, the tablets, on account of their greater convenience were resumed. The total urine for the 24 hours was examined. The microscopic examination showed results similar to that of No. 1., phosphates and occasionally carbonates were present. Crystals of calcium oxalate, which were not observed in Dog No. 1 were found twice in No. 2 during the normal period, but only once after the benzoate was begun. During the 2 gram period from April 23 to May 6 the urinary sediment was increased in bulk and appeared to be of a lighter and more flocculent character than before.

It was also noted that when the benzoate was discontinued, or during the after period, the urine took on a stronger and more offensive odor than before.

The chemical examination, as before, was upon the 24 hour urine and the averages of the different periods are shown in the following table :

	Amt.	Sp. gr.	Solids.	Chlor.	Sulph.	Phosph.	Urea.	Uric ac.	Sugar.	Alb.
Ave. of 3 exams. nor. per.	220cc.	1034	17.565	2.654	0.616	0.8690	9.83	0.0563	...	....
Ave. of 8 exams. 4 gm. per.	245cc.	1033.8	19.966	2.379	1.133	1.144	8.23	0.0825	0.437%	trace
Ave. of 3 exams. 6 gm. per.	293cc.	1036	23.716	2.547	2.188	1.345	7.23	0.088	0.50%	....
Ave. of 6 exams. 2 gm. per.	379cc.	1026	19.350	2.251	0·725	1.552	7.94	0.083	0.277%	....
Ave. of 3 exams. after per.	277cc.	1020	12.551	1.402	0.72	0.963	6.96	0.062	....	....
Max. of nor. per.	250cc.	1038	22.135	3.236	0.875	1.047	10.00	0.06	....	....
Min. of nor. per.	200cc.	1032	14.91	2 157	0.475	0.551	9.5	0.529	....	....
Max. of 4 gm. per.	340cc.	1044	25.24	3.351	2.50	1.733	11.56	0.1128	0.8%	....
Min. of 4 gm. per.	130cc.	1025	7.572	0.901	0.42	0.597	3.38	0.0309	0.2%	....
Max. of 6 gm. per.	350cc.	1046	24.465	3.051	3.850	1.516	7.70	0.110	0.56%	....
Min. of 6 gm. per.	220cc.	1030	23.113	2.030	0.700	1.221	6.51	0.074	0.48%	....
Max. of 2 gm. per.	710cc.	1040	24.232	3.352	1.485	3.355	10.00	0.106	0.37%	....
Min. of 2 gm. per.	180cc.	1014	13.630	1.386	0.160	0.725	5.40	0.54	0.185%	....
Max. of after per.	350cc.	1022	14.352	1.618	0.92	0.970	8.40	0.072	....	....
Min. of after per.	200cc.	1016	10.252	1.078	0.56	0.955	5.20	0.049	....	....

It is worthy of note that the normal urine of this dog contained no albumin, but that soon after the administration of the benzoate traces of it appeared upon two occasions, March 31st and April 4th, and then disappeared and was not found again during the experiment. After the benzoate was begun, the tests for sugar became quite pronounced ; this substance was evidently correlated with the benzoate, for when the latter was given in

decreased amount the sugar also decreased, and when the benzoate was discontinued the sugar also disappeared.

The effect of the benzoate upon the urine as a whole was to increase its amount and to cause an increase in the solids, particularly in the sulphates, phosphates and uric acid, while on the other hand the urea was decreased, as were also the chlorides to a slight extent. A comparison of the results obtained from the two series of urinary examinations, shows that there was, at least, a temporary disturbance of metabolism, because in both cases albumin—or in dog No. 1 more albumin—appeared just after the administration of sodium benzoate. The fact that the albumin soon disappeared or diminished would indicate that the metabolic processes soon adjusted themselves to the new conditions. Of more profound significance, however, was the presence of sugar. where a more direct and complete connection with sodium benzoate seemed to be established ; the inference being that the benzoate caused an interference with the metabolism of the liver. At any rate sugar appeared while the benzoate was administered, and diminished or disappeared when the benzoate was withdrawn.

In dog No. 1 there was not only an increased quantity of urine during the benzoate period but also an increase in the specific gravity and all of the urinary constituents. In dog No. 2 there was also an increase in the quantity of the urine as well as in the amount of the solids, sulphates, phosphates and uric acid ; but a decrease in the chlorides and urea.

The after period, when no benzoate was given, as compared with the normal, showed a slight increase in the sulphates, phosphates, uric acid and the quantity of urine passed, while the specific gravity, solids, chlorides, and urea were materially decreased.

The weight of dog No. 1 at the end of the experiment was 41.25 lbs. as against 40.50 lbs. the day the benzoate treatment began, showing a gain of 0.75 lb. A week before the treatment, however, the dog weighed 42 lbs.

The weight of dog No. 2 at the end of the treatment was 41.50 lbs. On the first day of the treatment it was 40.50 lbs., showing a gain of 1 lb. Like No. 1 a weighing was taken a week before the treatment and was then found to be 41.50. A

weighing was also made toward the close of the experiment, April 27th, and found to be 41.50 lbs. From the end of the treatment May 8th when the weight was 41.50 lbs. to May 17th when the dog was killed, it was found there had been a gain of 1.25 lbs., as the weight at the time of death was 42.75 lbs.

Examination of the blood of the two dogs was made by Dr. J. Traum. These examinations were made in the normal period, and during or just after the benzoate period. The following results were obtained :

	Red Corpuscles per cubic mm.	Leucocytes per per cubic mm.	Percentage of Hemoglobin.
Dog No. 1. March 24, '05. Normal period.	5,600,000	10,987	90
April 6, '05. End of benzoate period.	5,804,000	17,345	—
Dog No. 2. March 18, '05. Normal period.	5,988,000	7,499	92
April 13, '05. Near end of 4 gm. period.	6,195,500	7,162	91
May 9, '05. 3 days after end of benz. period.	6,126,000	8,050	100

The changes in the blood are not pronounced, except perhaps the leucocytes in dog No. 1 ; but such as they are, they favor the benzoate period. In dog No. 1 there is an increase in the red corpuscles (204,000) and in the leucocytes (6358). In dog No. 2 there is an increase in the red corpuscles during the benzoate period (207,500) and a decrease in the leucocytes (336). The after period compared with the normal also shows a slight increase in the red corpuscles (138,000) and something of an increase in the leucocytes (551).

The post-mortems on the dogs were performed by Dr. S. H. Burnett, of the Department of Pathology, New York State Veterinary College, who has kindly submitted his findings in the following notes :

" Post-mortem examination. Dog No. 1.

Dog killed by chloroform April 6th, 1905.

Skin scurfy, with hair partly fallen out.

A few translucent nodules, about 1 mm. in diameter, scattered over the surface of the left lung.

The right testicle retained in the abdominal cavity, flabby, flattened, size 1 by 2½ cm. The left one normal in appearance, 3 by 3 by 5 cm.

The other organs apparently normal.

Histological examination :

Liver. There is advanced parenchymatous and fatty degeneration of the liver cells except those in the periphery of the lobules immediately about the blood vessels.

Parenchymatous degeneration of the epithelium of the bile ducts. Moderate congestion of the veins and capillaries.

Kidney. Extensive parenchymatous degeneration of the epithelium in both cortex and medulla is shown, most marked in the convoluted tubules. There are a few purulent areas in the cortex. Congestion is shown in the glomeruli and capillaries between the tubules in the cortex and in the veins.

Lung. The nodules present just beneath the pleura are composed of a center of old connective tissue showing degeneration, while the outer part is more cellular. The lung near the nodule shows marked congestion ; farther away it is normal.

These changes in the liver, kidney and lung are chronic ones, evidently having existed for some time."

"Post-mortem examination, Dog No. 2 :

Dog, adult female, killed by chloroform May 17th, 1905. Considerable amount of subcutaneous fat. The organs were apparently normal except that there was a cyst ½ by 1 cm. in the anterior end of the left kidney and the duodenum contained four tape worms (Taenia coenurus?) 50—75 cm. in length. The dog had been spayed.

Histological examination :

Liver. All the blood vessels were congested, probably hypostatic. There was slight parenchymatous degeneration of the liver cells throughout the lobules.

Kidney. There was congestion of the blood vessels, prob-

ably hypostatic. There was a slight parenchymatous degeneration of the epithelial cells in the medulla and in the convoluted tubules."

The first experiment on man consisted of the administration of 5 grains of benzoic acid in a capsule three times a day before each meal. A general feeling of depression appeared to result from the use of the drug. There was a dull headache and dull but rather continuous pains over the region of the kidneys. The appetite and tone of the stomach appeared to be lessoned. One week before the benzoic acid was taken, was allowed for the normal period. The urine was collected for each 24 hours and a sample of this was taken for analysis. The same plan, regarding the urine, was pursued the following week when the benzoic acid was taken. The following averages show the results for the normal and benzoic acid periods :

	Amt.	Sp. gr.	Solids.	Chlor.	Sulph.	Phosph.	Urea.
Average of 7 exams. normal period.	846.4 cc.	1026.85	52.27	15.25	1.37	1.51	26.54
Average of 7 exams. benzoic acid per.	824.2 cc.	1026.85	51.25	13.68	1.44	1.39	23.75
Maximum of normal period	1000 cc.	1030.	64.65	18.46	2.30	1.85	30.00
Maximum of benzoic acid period.	1070 cc.	1030.	59.81	18.19	1.70	1.53	28.90
Minimum of normal period.	700 cc.	1022.	45.37	12.44	0.90	1.35	17.50
Minimum of benzoic acid period.	700 cc.	1024.	42.35	10.35	1.05	1.12	19.50

A comparison of the averages of the normal and benzoic acid periods shows that the sulphates were slightly increased during the latter period, but that all of the other constituents and the quantity of the urine were slightly greater during the normal period.

The subject of this experiment, Mr. M., was 27 years of age and was apparently enjoying the best of health. No evidence of albumin nor sugar appeared in the urine either before, during, or after the experiment.

The second subject, Mr. F., was 40 years of age and apparently in good health. In this case there was a normal period of 5 days, a benzoate period of 6 days, and an after period of 4 days. Ten grains of sodium benzoate were taken three times daily at each meal making the total dosage 30 grains or 2 grams per day. On two of the days 15-grain doses were taken, making a total of 45 grains or 3 grams per day. No physical effects whatever were apparent from the use of the drug. The appetite was in no way affected and the subject appeared to enjoy his usual health throughout. The following table shows the averages for the three periods above mentioned :

	Amt.	Sp. gr.	Solids.	Chlor.	Sulph.	Phosph.	Urea.	Ur. Ac.	Body Wt.
Ave. of 5 exams. nor. per.	1506cc.	1023.6	81.99	19.619	3.222	2.518	31.67	0 3995	185 4
Ave. of 6 exams. ben. per.	1745cc.	1023.8	95.11	21.883	3.895	5.244	33.76	0.2902	185.6
Ave. of 3 exams. after per.	1425cc.	1024.25	79.19	20.184	2.539	2.585	28.20	0.3009	185.7
Maximum nor. per.	1740cc.	1027.	85.13	22.467	3.690	3 390	33.75	0 540	186
Minimum nor. per.	1230cc.	1021.	77.37	17.335	2.610	1.674	29.52	0 2436	185
Maximum ben. per.	2280cc.	1029.	105.40	26.81	4.560	7.432	38.28	0.4700	186
Minimum ben. per.	1440cc.	1018.	81.99	17.557	3.360	2.169	29.83	0.2140	185
Maximum after per.	1590cc.	1029.	83.88	22.397	3.000	3.130	31.50	0.4698	186.25
Minimum after per.	1080cc.	1022.	72.87	16.642	2.667	1.907	26.01	0.1850	185.25

A daily record of the body weight was also kept throughout the experiment and the results show there was a slight gain (0.3 lb.) at its termination. No albumin or sugar was found in the urine at any time. A general comparison of the three periods of this experiment shows that during the benzoate period there was some diuresis and an increased amount of all of the constituents except uric acid, which was decreased about one-fourth. The phosphates were a little more than doubled in

quantity. The results obtained in the after period agreed more closely with the normal than with the benzoate period. In comparing the two experiments on man, it is shown that the only result in common during the benzoate period is a slight increase in the sulphates eliminated. In the one case (Mr. M) only 1 gram of benzoic acid was consumed daily while in the other case 2 grams and a portion of the time, 3 grams, of sodium benzoate were taken during the day. The difference in the drug and dosage may have some influence upon the result, otherwise it may be charged up to personal idiosyncrasy. A somewhat similar but not so marked difference in results is noted in the case of the two dogs. In dog No. 1 with larger dosage, there was, during the benzoate period, an increase in the urine and all of its constituents. In dog No. 2 there was a slight decrease in specific gravity, a decrease in the chlorides and urea but all of the other constituents were increased as in No. 1. In the case of Mr. F and dog No. 1 there is a correspondence in the results—an increase of the urine and all of its constituents, except that in Mr. F. the uric acid was diminished while in the dog it was increased slightly. This constituent was increased in both dogs. Unfortunately the uric acid was not tested in Mr. M. Urea was increased in Mr. F. and dog No. 1, while it was decreased in Mr. M. and dog No. 2. Diuresis, increased solids and phosphates occurred in all but Mr. M. The one result in which all four experiments agreed was an increased elimination of sulphates.

The general results seem to warrant the conclusion that sodium benzoate stimulates metabolism of the body and increases the elimination of the most of the waste constituents of the urine. This effect is probably dependent to some extent upon the dosage, for in the case of Mr. M. where the smallest amount of the drug was ingested there was a slight decrease in elimination.

SUMMARY.

The results of the experiments on the dog and man point toward increased metabolism and elimination of urinary products after the ingestion of moderately large doses of sodium benzoate. In all there was increased elimination of the sulphates. In three there was diuresis also an increase in the solids and

phosphates. In two there was an increase in the chloride and urea, while in the other two there was a decrease in the same constituents. In the two dogs there was an increase in the uric acid, one of them showing at the same time an increase in urea, while the other dog showed a decrease in the same constituent. In one of the men there was a decrease in uric acid; in the other it was not tested for. Both dogs with larger dosage than the men, showed a disturbance in metabolism during the benzoate period by the presence of albumin and sugar in the urine.

Sodium benzoate appears to stimulate the liver and general metabolism and increases the elimination of certain of the urinary products and causes some diuresis. These effects are undoubtedly correlated with the dosage ; the larger doses producing more marked results and the smaller doses less. The experiments showed a variation in the elimination of some of the more important of the waste products; e. g. urea, uric acid and chlorides. In some there was an increase and in others a decrease. Similar variations would doubtless exist in the human family due perhaps to personal idiosyncrasy or varying systemic conditions.

Large amounts of sodium benzoate, sufficiently long continued, may produce a disturbance of health, by interference with the liver ; with the digestive processes or undue stimulation or irritation of the kidneys as shown by its diuretic effect.

The effect of sodium benzoate upon the blood is not pronounced. The evidence from the experiments is that the red corpuscles were slightly increased ; the white corpuscles were somewhat variable, but upon the whole the number was increased and the hemoglobin was somewhat improved. The total effect is of a favorable character rather than otherwise.

The postmortems of the two dogs showed deviations from the normal, especially in connection with the microscopical examination of the tissues. Especial attention was paid to the liver and kidneys, because the most of absorbed material is carried through the portal system to the former and the latter are concerned with the elimination of the most of the waste products.

The findings in dog No. 1 will, doubtless for the most part, have to be left out of consideration, because in the opinion of the

pathologist, the lesions were of a chronic character and antedated the beginning of the experiment. The fact, however, that more albumin and sugar were found in the urine during the benzoate period than before, would indicate that the conditions were made worse rather than better.

In dog No. 2, the conditions were not so bad. The congestion of the vessels may have occurred as a result of the post-mortem settling of the blood or to the administration of chloroform in killing the animal. A brief administration of chloroform can hardly be considered as sufficient to produce the degenerative changes found in the liver and kidneys, for which a longer time must have been required. Although it is impossible to prove that these changes may not have existed before the experiment was begun, it is not improbable that they may have been due to the effects of the sodium benzoate, especially when taken in connection with the fact that albumin and sugar were found in the urine shortly after the benzoate treatment was begun. The albumin was found for a short time only ; the sugar persisted as long as the benzoate treatment was kept up, and disappeared when the benzoate was discontinued. The dosage, averaging 4 grams (60 grains) daily continued for some time, may have been rather large for a dog of that weight (41 lbs.), and it is reasonable to assume that smaller doses would have produced less violent changes. The smaller doses, 1 gram and 2 grams daily, in the experiments on man, did not cause the appearance of albumin or sugar in the urine.

ALBUMINURIC VARIATION AT THE BEGINNING AND END OF MICTURITION.

PIERRE A. FISH AND THOMAS SHELDON.

The patient, a man of 29 years, had been afflicted with albuminuria for a number of years. During the urinary examinations the idea was suggested that it would be well to determine if the albumin were uniformly distributed throughout the urine while in the bladder.

The results are shown in the following table. Variations in the amount of albumin on different days and its complete disappearance at the end of the experiments were probably due to treatment for the disorder. No treatment was taken at the beginning of the experiment.

The ferrocyanide-acetic acid test was used in connection with the centrifuge. The value of each 0.1 cc. of the precipitate was determined in order to obtain quantitative results. Ten cubic centimeters were taken from the first urine passed, and the same amount was also taken from the last to leave the bladder. This amount was placed in the centrifuge tube with the ferrocyanide and acetic acid and both tubes revolved in the centrifuge for three minutes.

	First Urine.	Last Urine.
Feb. 8, 11:00 A. M.	Tube No. 1, .99 gm.—1000.	Tube No. 2, .44 gm.—1000.
Feb. 9, “	“ “ .66 “ “	“ “ .22 “ “
Feb. 11, “	“ “ 1.44 “ “	“ “ .51 “ “
Feb. 12, “	“ “ 1.22 “ “	“ “ .44 “ “
Feb. 12, 2:00 P. M.	“ “ .22 “ “	“ “ .22 “ “
Feb. 13, 11:00 A. M.	“ “ .33 “ “	“ “ .22 “ “
Feb. 14, 12:00 M.	“ “ .28 “ “	“ “ .11 “ “
Feb. 14, 5:00 P. M.	“ “ .77 “ “	“ “ .22 “ “
Feb. 15, 5:00 P. M.	“ “ .22 “ “	“ “ .22 “ “
Feb. 21, 3:30 P. M.	“ “ .002 “ “	“ “ faint trace.
Feb. 23, 3:00 P. M.	“ “ .08 “ “	“ “ .002 gm—1000.
Feb. 27, 12:00 M.	“ “ .11 “ “	“ “ faint trace.
Feb. 28, 2:00 P. M.	“ “ .00 “ “	“ “ .00 gm.—1000.
Mar. 2, 3:30 P. M.	“ “ .02 “ “	“ “ .00 “ “
Mar. 4, 11:30 A. M.	“ “ .00 “ “	“ “ .00 “ “

The reason for this variation we do not attempt to explain. In none of the fifteen experiments was a larger amount of albumin found in the last urine than in the first. In two instances the same amount was found in each urine, but in the thirteen remaining tests quite markedly larger quantities of albumin were found in the first urine. Diurnal variations in the amount of albumin are very probable, but as shown by the table the tests were made at different hours on different days, and there is, nevertheless, quite constant variations in the amount of albumin in the initial and final urine of each micturition.

PIERRE A. FISH.

ABSTRACTS

OF

WORK DONE IN THE LABORATORY

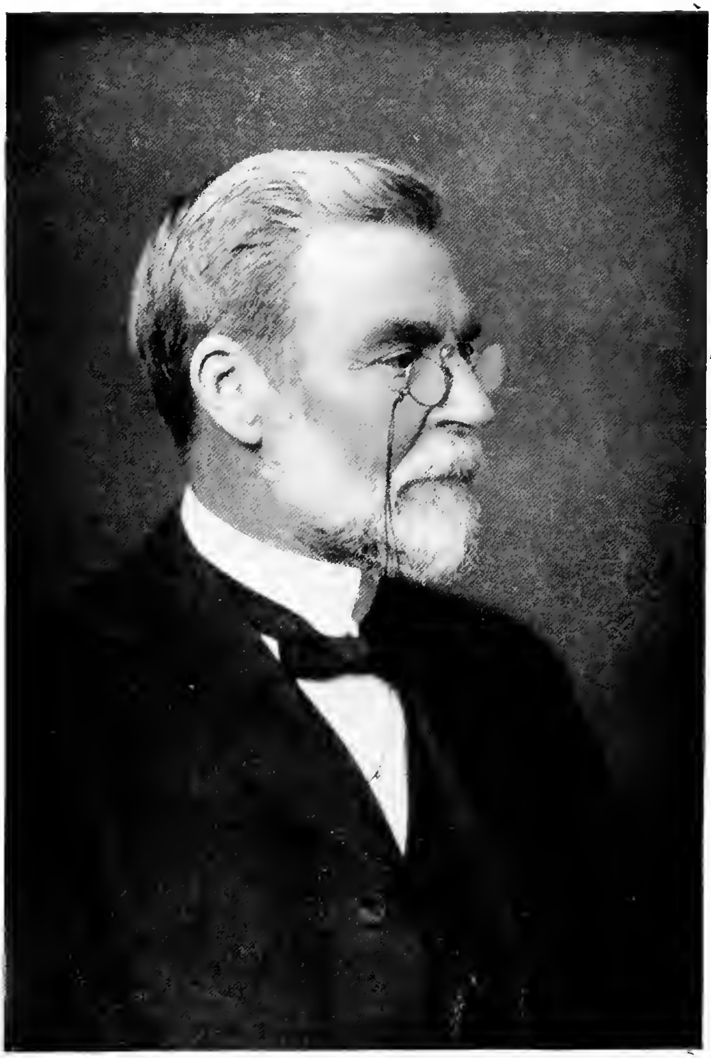
OF

VETERINARY PHYSIOLOGY AND PHARMACOLOGY

UNDER THE DIRECTION OF P. A. FISH

NO. 5
NEW YORK STATE VETERINARY COLLEGE
CORNELL UNIVERSITY
ITHACA, N. Y.
1908

TABLE OF CONTENTS.



DR. LAW'S SERVICES TO THE VETERINARY PROFESSION.

PIERRE A. FISH.

When such men as Professors Law and Gage leave the faculty it sets one thinking, especially such of us as have been fortunate enough to have been associated with them as students, assistants and colleagues.

A learned judge once said that he believed that it would be for the best interest of all concerned if the judge who sentenced criminals should spend a certain time in prison himself before entering upon the duties of his high position. In this way he would more thoroughly appreciate the degree of punishment he was inflicting and could thereby temper his judgment with mercy as well as justice. I do not fear contradiction when I say that Dr. Law, with his long experience as student and teacher, has never been charged with injustice by any of the numerous students he has taught.

When Dr. Law began his career in this country forty years ago he found very few veterinarians, but a large number of horse doctors. No diploma was required in those days. Any stableman or member of the saloon contingent, merely by announcing his intention, could treat sick animals. There were no illegal practitioners, simply because there were no practice laws for them to break. Such a class of practitioners, largely illiterate and too indolent to take up any other useful work, were not held in very high esteem by the community.

The importance of animal diseases to the stock owner and to the community at large became more and more emphasized, so that the subject was taken up as a part of the instruction in agricultural schools and experiment stations. The evident result of this instruction was to enable the farmer to treat his own animals. This course may be considered justifiable under the old conditions when competent veterinarians were not available.

The aim at the present time is to elevate veterinary work to the dignity of the learned professions. In this direction numerous stakes have already been driven along the line of progress. Within recent years a few of our states have made more or less liberal appropriations for fostering veterinary education. A number of the states have

enacted laws which prohibit those not properly qualified from practising veterinary medicine. Educational requirements have been raised, so that to enter the veterinary schools in New York state as much education is required as to enter many of the medical schools of our country.

With the increasing efficiency of the veterinary profession there come increasing problems. One of these is intimately connected with the agriculturalist. It may be said that if it were not for the farmer to breed the domestic animals there would be no veterinarian to treat them. While this is, in a sense, true, it is also true that other professions and, in fact, all, whatsover their line of life, are dependent for their sustenance upon the soil and the man who tills it—upon him who tickles the face of the earth until she smiles back at him with her abundant harvests.

Should the veterinary college serve as a bureau for the diffusion of information to the farmers generally for any and all diseases with which their animals may be affected? Should this be the principal function of the veterinary college, or should it send out thoroughly trained men upon whom the farmers may call in case of need? It is eminently proper for the veterinary school to furnish to the farmer fully and freely all of the information it can in respect to sanitary and preventive medicine, but information relating to infectious and special diseases he should receive through the veterinarian. It would obviously be an absurd procedure for a college to devote its energies to developing professional veterinarians and then put them out of business by encouraging the farmer to be his own veterinarian. "Every man his own doctor" is now an obsolete condition. The veterinary college may exercise a dual function. It should serve as a school for the training of professional veterinarians and developing knowledge of sanitary and preventive medicine.

We may, then, trace these three phases in the development of the veterinary profession: 1st, the "horse doctor" period, characterized by the absence of legal restrictions, when anyone so inclined might take up the work according to his own desires. 2d, the agricultural period, when the veterinary work was an appendange of agricultural instruction. 3d, the professional period, which we are at present developing into, striving to stand upon the level of the sister profession—human medicine.

Our present director is familiar with all of these periods. His services have been sought by the community, state and nation. The changes wrought in forty years cannot be attributed to any one man, but as much, if not more, of this influence can be traced to Dr. Law as to any other. Not least among his services to the profession is the production of his text books on veterinary medicine, prepared during the strenuous period of organizing and directing the New York State Veterinary College. In the words of Horace, he has reared "a monument more lasting than brass."

But in the final analysis it seems to me, as a culmination of his services, the chief legacy which he leaves to posterity is his directorship of a school through which he has emphasized and dignified the professional side of veterinary medicine—a school to enter which a person must possess at least a high school education. Aside from character there is no quicker or more satisfactory method of elevating the veterinary profession or for the veterinarian to win the esteem of the community than for the public to know that it requires as much education for a young man to enter a school of veterinary medicine as it does to enter most schools of human medicine. The path of the truly great man is not strewn with roses. There are always those who criticize and endeavor to block the wheels of progress, and Dr. Law has not, perhaps, been exempt from trials of this character.

The story is told of an officious captain of a small boat plying along the eastern coast, who hailed everything in sight, demanding the name and destination of the vessel. One day he sighted a large and stately vessel and true to his instincts he ran alongside, donned his gaudy uniform, mounted the bridge of his little boat and got off his usual salutation. The reply from the other captain, in his faded uniform, was to the effect that he was some months out from an Asiatic port on a trip around the world; that his vessel was laden with spices and rich merchandise and that he was homeward bound.

Our director is homeward bound, laden with years and his many services to the veterinary profession. May the remainder of his voyage be peaceful. May he finally enter the home port safely and gently—but not too soon.

A toast given at the fifth annual banquet of the Society of Comparative Medicine, Feb. 20, 1908, upon the approaching retirement of Dr. Law as Director of the New York State Veterinary College.

PROFESSOR GAGE'S WORK FOR THE VETERINARIANS.

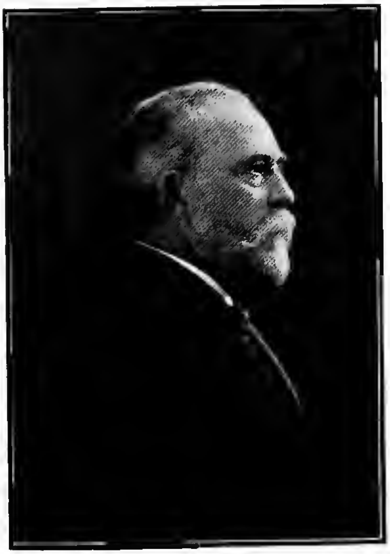
G. S. HOPKINS.

Two years ago I had the honor of giving a sketch of the alumni of the College. On that occasion I felt free to use as vivid colors as I pleased. The alumni were not present, to pass judgment, and even if they had been and failed to recognize their own likeness, I might have replied that it was a composite, and therefore not necessarily true of any individual; and yet it was essentially all true. I was equally secure, also, from those who were present at that time, for to most of them the alumni were unknown.

Now, it is quite a different matter. Not only is the subject of my sketch present, but he is well known to all of you; and is not my immediate background "twenty-five years in the harness," and this will hardly permit of any but the most subdued colors.

The relations of Professor Gage to the veterinarian have been mainly those of teacher and pupil; indirectly, however, he has had a share in starting a reform movement which ultimately, I believe, will revolutionize all of our veterinary schools.

When our College was opened in 1896, Professor Gage was appointed Professor of Histology and Embryology in the Veterinary College and the College of Arts and Science. Prior to that time he was Associate Professor of Histology and Embryology in what was then called the Anatomical Department. He remained an active member of the Veterinary College Faculty for about five years, when he was transferred to the Medical College. As a member of the Veterinary Faculty he was influential in fixing the entrance requirements and the courses of study. At about this same time the State Legislature enacted a law fixing the minimum requirements for the practice of veterinary medicine in this State. Just what influence, direct or indirect, he had in this I do not know. A few years later the requirements for entrance to the college were raised from two to four years of high school work. As a result of these added requirements for admission to the two colleges of this State, the reform movement just alluded to was brought to the attention of everybody in the country interested in veterinary education. Many excellent men are strongly opposed to the



Simon H. Gage

present requirements, but, on the other hand, there are a great number who are convinced that it is high time that the members of the profession begin to fit themselves more adequately for the crowding opportunities of splendid service to the community, to the state and to the nation.

The present four-year high school requirement is bu the first step in this reform movement; a four-year college course probably will be the second step and then still higher entrance requirements. But these advances alone will not solve the problem. In addition to better general education, and better technical training, there is needed in all branches of veterinary science men who have the ability and the disposition to study and observe actual things and conditions, as well as to stndy about them. Right here, to my mind, lies the secret of Professor Gage's inestimable service to all students privileged to take work with him. They are given every opportunity to see and to think for themselves, and are encouraged, by precept and example, to make the attempt. If they fail to catch something of the spirit of their teacher, it is only because they are not attuned to the high notes which many of his former students have heard and responded to, even if in a minor key.

Every one in the Veterinary College is, just now, more or less interested in Art and things artistic. Someone has said that Art is the expression of a man's joy in his work, and that all of the joy and high purpose he weaves into the fabric comes out again and influences him who has the soul to appreciate. Whether or not this be true, it is true that both of the teachers who have taught all of our students, but who alas, will teach them no longer, do express in their teaching and example the joy they find in their work; it is true that something of the high purpose exemplified in them does touch a responsive cord in the heart of every one of their students; it is true, as all here will agree, that the fabric of life each of them has thus far woven may be summed up in these borrowed words: "A noble life is not a blaze of sudden glory won, but just the summing up of days in which good work is done."

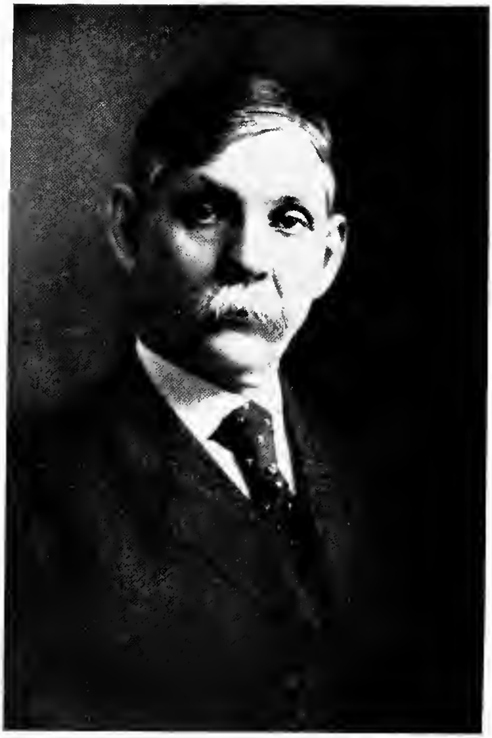
A toast given at the fifth annual banquet of the Society of Comparative Medicine, Feb. 20, 1908, upon the approaching retirement of Professor Gage.

THE NEW DIRECTOR OF THE N. Y. STATE VETERINARY COLLEGE.

At the meeting of the Trustees last February, Veranus A. Moore, Professor of Veterinary Pathology, Bacteriology and Meat Inspection, was appointed Director of the New York State Veterinary College, to succeed Dr. James Law upon his retirement from active work at the next Commencement in June. Dr. Moore continues his work in the department with which he has been identified since the opening of the college. The executive and administrative duties of the directorship are added to his usual work.

Dr. Moore received his B. S. degree from Cornell in 1887, and the degree of M. D. from the Columbian University in 1890. While in Cornell University his interest lay especially along biological lines and a large proportion of his time was spent in the departments of botany and histology, where an excellent foundation was laid for his later work in Washington. Near the time of his graduation he accepted a position in the Bureau of Animal Industry upon the invitation of Dr. D. E. Salmon. He was associated for a number of years with Dr. Theobald Smith in the Division of Animal Pathology. When Dr. Smith left the government service to accept a professorship at Harvard University, Dr. Moore succeeded him as chief of the division. He was in this position, however, for only one year, resigning in the fall of 1896 to accept his present professorship at the then newly organized State Veterinary College at his alma mater.

Dr. Moore's researches upon important questions relating to animal diseases, while in the service of the government, have made him widely and favorably known in veterinary and scientific circles. Since his connection with the State Veterinary College his reputation in this respect has in no way diminished. The publication of the results of numerous important investigations and high grade text books pertaining to his subjects show his great activity. His counsel and advice have been widely sought throughout the state in connection with the prevention, diagnosis and sanitary control of outbreaks of animal diseases. His laboratory, in addition to its use for purposes of instruction, is the scene of considerable activity in the preparation



Dr. V. A. MOORE

of tuberculin, mallein anthrax vaccine and other diagnostic and curative agents for the use of veterinary practitioners. A rapidly growing feature of his department is the increasing number of tissues sent in for the diagnosis of the various infectious dieases.

The appointment is a well deserved one. Under the broad-minded administration of Dr. Moore a period of even still greater usefulness is predicted for the New York State Veterinary College.

P. A. F.

OBSERVATIONS ON THE VETERINARY SCHOOLS IN EUROPE

PIERRE A. FISH.

During a recent visit to Europe, twelve veterinary colleges distributed throughout six different countries were visited. There were varying conditions in these countries, and as the methods and customs were quite different from those in America a brief description may be of some interest.

In the order in which they were visited, the Liverpool Veterinary School comes first. This school forms part of the University of Liverpool. The course of instruction is four years long, each year being divided into three terms of about ten weeks. There are about sixty students. The requirements for entrance are English, grammar, arithmetic, algebra, geometry, Latin and one of the following optional subjects: Greek, or any modern language or logic. A note in their catalog for 1905-6, however, states that "as there is a probability in the near future of a university degree for veterinary surgeons, candidates are strongly advised to, if possible, pass a high standard preliminary examination—that is, one which will qualify for university graduation."

The tuition to cover the instruction is eighteen guineas, or a little more than $90 per year. The strictly veterinary portion of the work is carried on by Professor W. O. Williams and Professor Share-Jones, with assistants. For the remaining work the students mingle freely with the university medical students in the various departments.

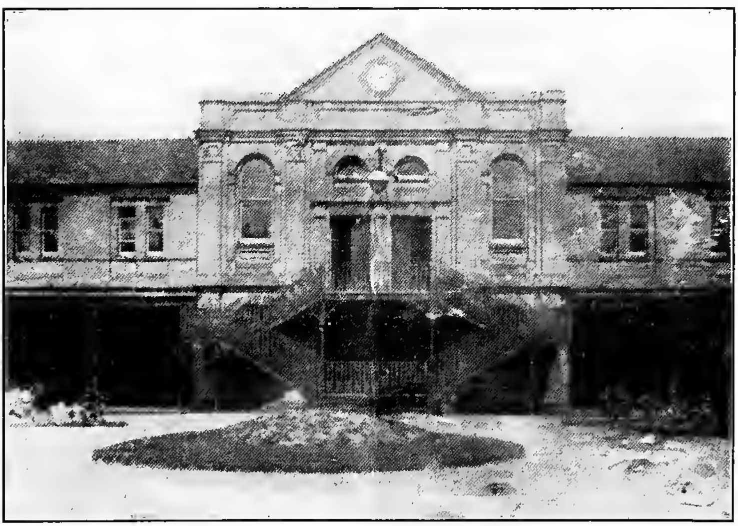
There is no clinic at the University, but the corporation of Liverpool has placed its horse depots, including over six hundred horses, and Veterinary Infirmary at the disposal of the veterinary staff of the school for the purposes of instruction. The students of the fourth year also attend the indoor clinics of some of the veterinary establishments in the city.

I understood also that veterinarians who were qualified might obtain the degree D. V. H., Doctor of Veterinary Hygiene, by devoting two terms to the study of the appropriate subjects at the University.

Canine Hospital, Liverpool.

Veterinary Ward, Liverpool.

Entrance to the Royal Veterinary College, London.



Royal Veterinary College, London. Court facing the entrance.

The Royal Veterinary College of London was founded in 1791, and incorporated in 1875. According to its latest catalog the University of London has recently instituted a Degree in Veterinary Science (B. Sc.). "The possession of this degree will not of itself entitle the holder to practise as a veterinary surgeon, but it is hoped that year by year an increasing number of students will, while studying for the diploma of the Royal College of Veterinary Surgeons, also adopt the curriculum which is necessary to qualify for the University examinations and obtain the degree of Bachelor of Science. In conformity with the statutes of the University, the Professors of Chemistry, Biology, Anatomy, Physiology, Hygiene and Pathology in the Royal Veterinary College are recognized teachers in the University."

Four years of study are required at the Veterinary School for a student to be eligible for the examinations given by the Board of the Royal College of Veterinary Surgeons. It is expected that an additional year must be taken in order to acquire the University degree.

The entrance requirements are much the same as for the school at Liverpool and include: English Language, Latin, Arithmetic, Algebra, Geometry and one optional subject, either Greek or one of the modern languages.

From Oct. 1 to about the middle of March there are two terms. A summer term begins May 1 and continues to about the middle of July.

A novel method for raising revenue exists in this college. A person or firm properly approved and elected becomes a "subscriber" to the college. Persons who contribute twenty guineas (about $100.00) in one sum are life subscribers, otherwise they pay two guineas (about $10.00) per annum and are entitled to the privileges of a subscriber so long as they continue their subscriptions. A subscriber has the following privileges: He may have in the course of any year five horses examined for soundness free of charge either before or after purchasing. Any additional horses are charged for at the rate of 10s. 6d. (about $2.50 each). He may have admitted into the infirmary for medical and surgical treatment an unlimited number of horses and other animals *his own property* at a charge only for their keep.

He may be supplied with medicine for *his own* animals at a fixed charge.

At a fixed rate he may have at the college a chemical analysis of any water, provender, oil-cake or other feeding material, or of the viscera and their contents of any of *his own* animals suspected of having been poisoned.

He may have the opinion of one of the professors without the payment of a fee as to the medicinal treatment of any of *his own* animals, brought for this purpose to the college, which he may desire to retain in his own keeping.

In cases of extensive or serious outbreaks of disease he may have an investigation made into its nature and causes with a view to its prevention or cure on payment of the fixed charges.

He may have a post-mortem examination of any animal, or parts of an animal, sent to the college, and receive an opinion of the probable cause of death on payment of a fixed charge.

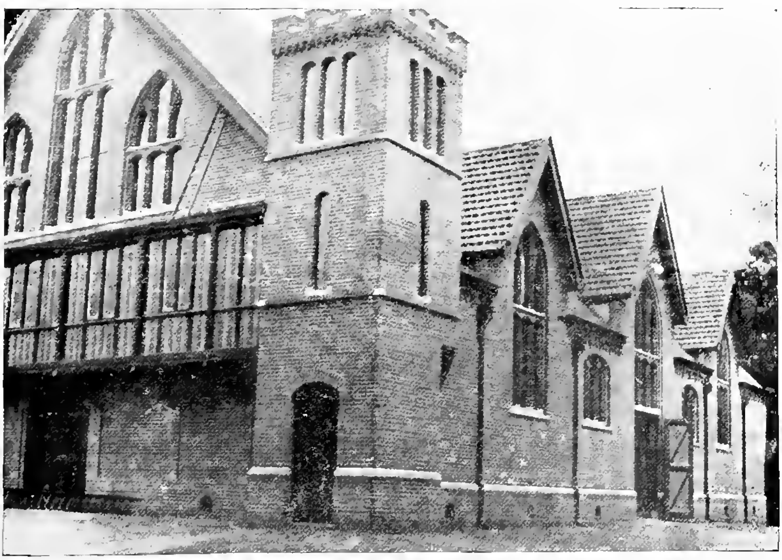
The professors are not allowed to examine horses as to soundness out of the college, nor visit sick animals except by special permission of the principal or professor in charge, and then only for the purpose of consultation with a veterinary surgeon or with the object of the removal of patients to the infirmary for treatment.

The sick animals of the subscribers constitute the internal clinic of the college. This clinic is under the direction of Professor Penberthy (medicine) and Professor MacQueen (surgery), each professor having charge two days alternately. The students do not participate in this clinic to any extent except as onlookers. There is also an external clinic which is in charge of Professor Woodruff—Materia Medica. There is a nominal charge of 1s. (25c.) to enter the patients in this clinic. A great many cases are examined here and the students of the fourth year take an active part in performing minor operations and keeping records. Two hours in the forenoon and two in the afternoon are devoted to the clinics.

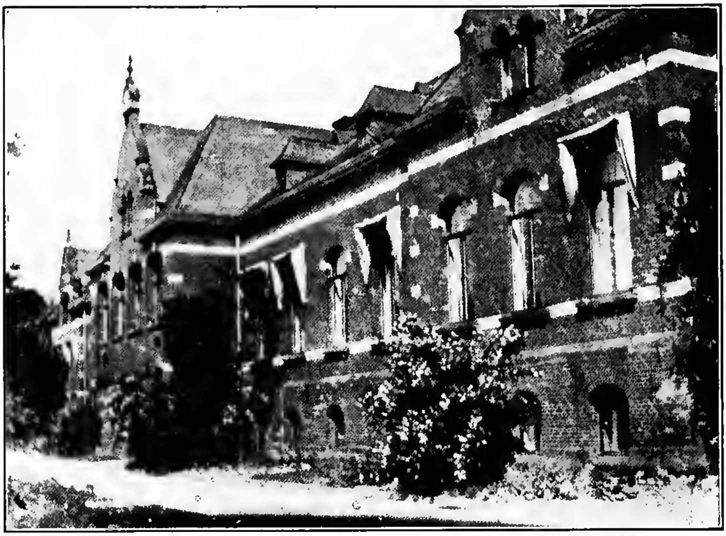
The tuition is twenty guineas a year (about $100.00). In addition there is a fee of 1 guinea to the library and reading room fund to be paid prior to entry and a further fee of 10s. 6d. annually. The number of students in attendance is about 200 and the number is diminishing. It is believed by some that the decreasing attendance is due to the automobile bus service in London.

The Veterinary School at Utrecht under the directorship of Professor Wirz is the only school of its kind in Holland. Like the schools

Veterinary Hospital and Lecture Rooms (upstairs), Utrecht, Holland.



New Judging Pavilion, Veterinary School, Utrecht, Holland.



Institute of Physiology and Chemistry (rear),
Veterinary School Hanover.

Building for Surgical Clinics, Hanover.

in England, it has a four-year course. There are quite extensive grounds with a number of buildings. There are about 140 students in attendance. The clinical hours are in the forenoon from 10 to 12. The clinics are free as to consultation and medicine, but there is a charge for the fodder that the animal consumes. I was informed that there was a good demand for veterinarians in Holland and that they did well.

Some idea of the work accomplished may be obtained by glancing over the following table, taken from the catalog of this school for 1904-5. The table represents the number of cases treated in each clinic during the period of one year.

	Stationary Clinic.	Consulting Clinic.	Ambulatory Clinic.	Total.
Horses and Asses	413	901	89	1403
Cattle	32	260	447	739
Sheep	—	5	1	6
Goats	12	57	3	72
Varkens (Swine?)	—	27	11	38
Dogs	223	1413	2	1638
Cats	—	296	—	296
Birds	—	422	—	432
Other Animals	68	—	—	68
	748	3391	553	4692

At Hanover, Germany, I found a comparatively new and beautifully arranged veterinary school in its group of botanical gardens. It was under construction from 1895 to 1899, and I was informed that its cost amounted to 4,000,000 marks ($1,000,000). About twenty buildings are included in these grounds, and it indeed surpasses in beauty and extent some of the smaller universities in the United States.

The entrance requirements, as I understand it, are the same throughout Germany. A student must have passed through a gymnasium (about nine years), which corresponds to a high school education and that which precedes it in the States.

The length of the veterinary course is seven semesters of about five months each, or a total of three and a half years. The tuition per year at Hanover is 160 marks ($40.00). An eighth semester is devoted to final examinations for those who are eligible and able to complete the course. For this semester no tuition is charged.

The medical and surgical clinics under Professors Malkmus and Frick, respectively, and the clinic for small animals under Professor Kunneman are well patronized. The students do not operate upon patients, but study them, dress wounds and keep records of their progress. Subjects are purchased for the students to operate upon and these are then utilized for dissection. In the clinic there is no charge made for consultation. Medicines are furnished at about 25 per cent. below the usual rates. A payment of 2 marks (50c.) per day covers everything in the surgical clinic.

There are about 240 students in attendance at the Hanover school.

Military service is compulsory in Germany and veterinarians are not exempt from it. Because of their higher education, and this applies to medical and university students also, only one year is required instead of two years as for ordinary individuals. A student must serve out his military term before he can embark in private practice. I was informed that the government would pay the expenses (not personal) of a student at a veterinary school, and in return would require him to serve from seven to ten years as an army veterinarian—at least one year for each semester.

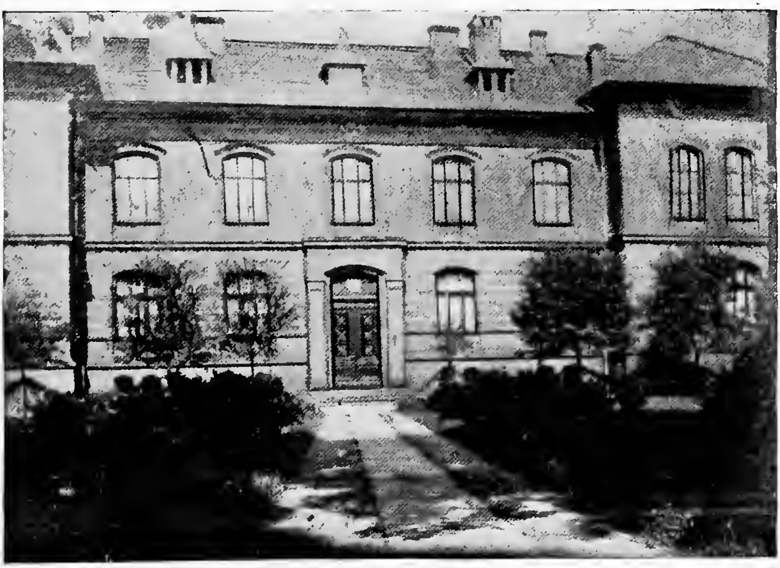
The veterinary school at Berlin leads all the others in the number of students, there being 335 in attendance. Berlin, I was informed, is a military school and the students attending there are preparing for service as army veterinarians. The grounds of the Berlin school are about as extensive as those of Hanover, and there are numerous new and modern buildings. Some of the older buildings are to be replaced by new ones in the near future. A number of the professors live in a building situated upon the grounds. This is true to a much less extent of the majority of the schools visited in Germany—either a professor or some of the assistants being furnished with quarters.

In addition to the medical clinic under Professor Fröhner and the surgical under Professor Eberlein, and the clinic for small animals under Professor Regenbogen, there is a very large polyclinic under Professor Karnbach. A great many animals are treated in these clinics.

Professor Zuntz, Director of the Agricultural School not far from the Veterinary School, but independent of it, has done some important work upon the physiology of the domestic animals.

The tuition is the same as at Hanover, $40.00.

Entrance to the Berlin Veterinary School. Statue of Gerlach.



Institute for Pathology, Berlin.

Department of Anatomy and Clinic for small animals, Dresden.

Department of Pathology, Dresden.

I was told as a matter of historical interest that Virchow as a young student did some work at the Veterinary School, and it was there that he discovered the bacillus of malignant oedema. Also that Koch's discovery of the Bacillus of Tuberculosis and the Comma Bacillus occurred in a building situated near the Veterinary grounds.

I am under considerable obligation to Professor Ostertag and his assistant, Dr. Himpel, for courtesies rendered in making it possible for me to attend various lectures and clinics not only in the Veterinary School but in the University of Berlin as well.

The following data relating to attendance and cases presented at the clinics at Berlin was taken from the Veterinary Journal for September, 1907, and relates to the year 1905-6.

"During the summer session 400 and during the winter 416 students were on the roll of the school, and 21 military students. One hundred and ten presented themselves for the final examination, of whom 97 passed.

One thousand seven hundred and twenty-seven horses and one donkey were treated in the medical wards under Professor Fröhner, and 760 horses in the surgical under Professor Eberlein. Six hundred operations were performed; six thousand nine hundred and thirteen large animals were attended as out patients under Professor Karnbach and 1908 minor operations were performed. In the canine ward, under Professor Regenbogen, 1260 patients were treated and 244 operations were performed. Eight thousand dogs, 181 cats and 14 monkeys were attended as out patients, and 632 minor operations were performed.

Post-mortem examinations were made by Professor Schütz on 305 horses, 1 donkey, 2 oxen and 113 dogs. Professor Eggeling paid 453 visits and treated 52 horses, 486 oxen, 561 pigs and 3 goats."

The grand total of all the animals treated in the various clinics amounts to 20,017.

The Veterinary School at Dresden, under the directorship of Professor Ellenberger, is not so extensive as those at Berlin and Hanover; but the buildings are well appointed and conveniently arranged. In a building upon, or adjoining, the grounds reside veterinarians in the military service who take a course of about six months in horse shoeing and the forge under Professor Lungwitz.

The clinics are conducted on a plan similar to that at Berlin, but

the charges for the patients are somewhat less. There are about 167 students in attendance. The tuition is 160 marks ($40.00) per year, with 10 or 12 marks additional for special purposes.

The Veterinary School at Munich, with Professor Albrecht as director, has buildings somewhat older than the other German schools, but they are well equipped and arranged. The building containing the pathologic collection of Professor Kitt is the most antiquated, but the collection is most interesting. I was informed that Professor Kitt had recently been retired on account of disability.

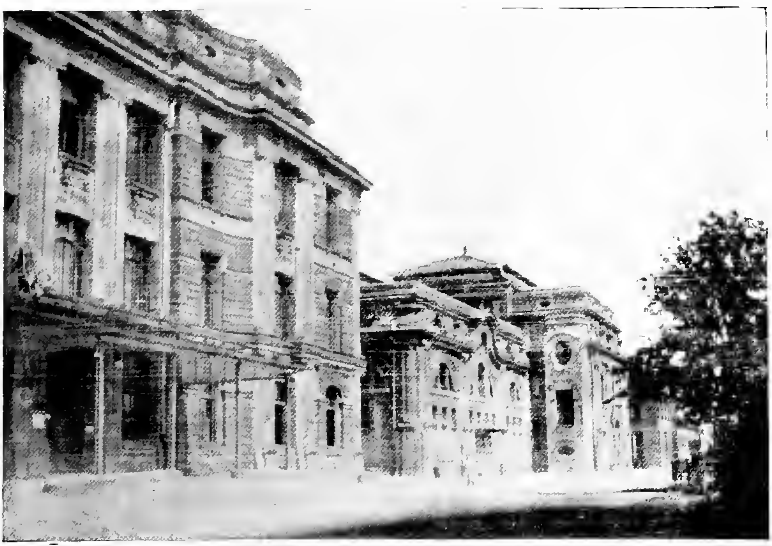
The tuition charges are only 60 marks ($15.00) a year at this school, and the clinical charges were also lower than at the other schools. The attendance is about 320.

According to the catalog for 1905-6 the Munich school received the following number of animals in their various clinics:

	Horses.	Ruminants.	Carnivora & Herbivora.	Swine.	Dogs.	Carnivora.	Cats.	Birds.	Other Animals.	Total.
Medical Clinics.	312	3	...	23	797	...	39	59	...	1233
Surgical Clinics Large Animals Diseased.	549	22	...	51	...	....	..	..	...	622
(Operated upon)	(412)	(21)	...	(51)	...	....	..	..	...	....
Surgical Clinic Small Animals Diseased.	...	...	23	..	...	1032	..	..	32	1087
(Operated upon.)	...	...	(20)	..	...	(712)	..	..	20	....
Polyclinic Surgical Division.	6	...	...	..	1831	....	78	..	52	1967
Polyclinic Medical Division.	36	...	...	..	2419	....	148	..	213	2816
Ambulatory Clinic.	194	618	...	1081	....	111	..	..	89	2093

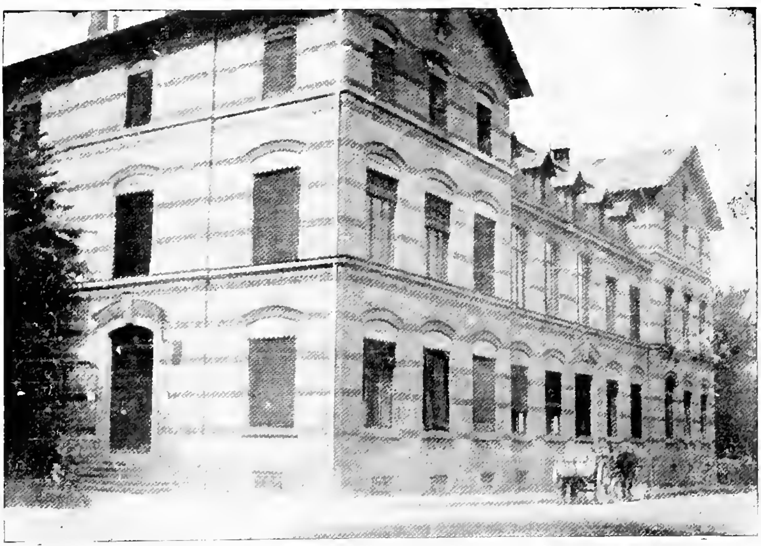
The Veterinary School at Stuttgart, under the directorship of Professor Süssdorf, has grounds about as extensive as those at Dresden and Munich. Some of the buildings are quite antiquated, but the Institute of Anatomy and Pathology and the departments of Medicine and Surgery are well quartered in relatively new and commodious buildings. There is quite an elaborate system for ventilating the hospital wards of both of these departments. The department of surgery under Professor Hoffman shows a wonderful range of mechan-

Entrance to the Veterinary School at Munich.



Buildings for Medical and Surgical Clinics, Munich.

Entrance to the Veterinary School at Stuttgart.



Building for Anatomy and Pathology, Stuttgart.

ical ingenuity in the arrangement and manipulation of its apparatus. There is an elaborate operating table regulated by hydraulic pressure. It may be turned to a vertical or horizontal position or tilted to any angle and may be raised or lowered by means of a lever. There is also an elaborate apparatus for confining a horse by means of a system of clamps for the head and neck—the feet being fastened to the floor. A large Roentgen Ray apparatus is also included in the equipment. The stalls are most conveniently and hygienically arranged for the comfort of the patients. Water is supplied to each stall automatically through a pipe, so that the patient has always a supply before him. There are from 120 to 150 students at this school, and the tuition is 140 marks ($35.00) per year.

It was a matter of much regret that time did not permit me to visit the Veterinary School at Giessen. I was informed that it had quite a close relationship to the medical department of the university—more so than any other school in Germany.

In Switzerland, the first school that I visited was at Zürich. Unfortunately the season for instruction ended at about the time I was there and I was unable to witness the work and meet as many of the professors during the remainder of the trip as previously.

This school is affiliated with the University of Zürich, although the school buildings are some distance from it. There is no separate director of the school, the president or director of the university officiating as such. A portion of the course, including botany, zoology, physics, chemistry and physiology, is therefore given at the university. The veterinary faculty is included with that of the university. The school is small, including only 35 students, and the buildings are somewhat old. The entrance requirements for the schools in Switzerland are similar to those in Germany.

There is also compulsory military service in Switzerland. It differs in some interesting ways from that in Germany so far as veterinarians are concerned. As it was explained to me, the young man, while still a student, must serve in the recruit school, devoting eight weeks to military service if in the artillery, or twelve weeks if in the cavalry. If he wishes to maintain some connection with the army he attends the under-officers' school (optional) for five weeks for the artillery branch. Then comes the officers' school (also optional) after the state examination, where he spends six weeks. Then

he becomes an officer-lieutenant and must serve eight weeks if in the artillery, or twelve weeks if in the cavalry. After the officers' school comes what is known as the "Wiederholens Kurs" (repetition), and the lieutenant must serve every second year for three weeks until he is 32 years of age. A lieutenant gets six francs, or $1.20, a day while serving.

The following report of the clinical work at Zürich for 1906 was furnished me during my visit.

	Hospital Clinic.	Ambulatory Clinic.	Consulting Clinic.	Total.
Horses	921	1089	3474	5498
Asses and Mules	1	—	13	
Cattle	38	1626	76	1740
Swine	2	92	205	299
Goats	—	8	3	12
Sheep	—	1	—	
Dogs	563	163	1933	2659
Cats	5	12	264	281
Fowls	—	47	10	
Parrots	1	1	2	84
Other Birds	1	—	22	
Rabbits	1	—	10	
Gninea Pigs	—	—	2	14
Squirrel	—	—	1	

The remaining Swiss Veterinary School is at Berne and is affiliated with the university of that city, although the buildings are separate. This school is larger than the one at Zürich, having 45 students. The grounds are somewhat larger and the buildings are more modern and commodious.

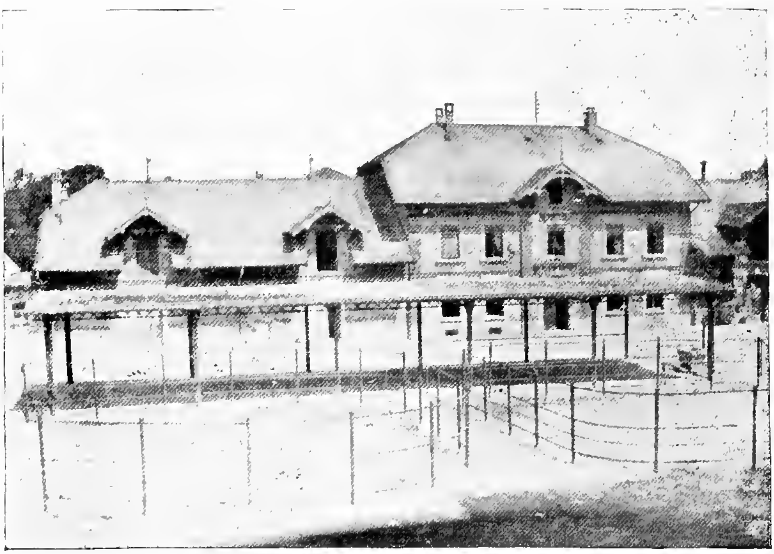
The veterinary faculty is included with the university faculty. The Swiss, like the other schools, have clinical periods during the forenoon. The tuition in both schools is from 200 to 300 francs ($40.00 to $50.00) per year. The course in both schools is four years long.

Through the kindness of Dr. Liautard, who accompanied me, I obtained a very fair idea of the school at Alfort, Paris, although the work of instruction had ceased. The grounds with their pleasant groves and numerous buildings are very extensive and contain statues of Bourgelat and Bouley and a bust of Nocard. A few of the older buildings still remain.

Veterinary Hospital, Zürich.

Administration Building, Lecture Rooms, etc., (rear) Zürich.

Veterinary School, Berne.



Veterinary Hospital and Grounds, Berne.

The clinic continues through the vacation and presented a scene of considerable activity at the time of my visit, many of the students remaining to assist. There are between 250 and 300 students in attendance and they take their clinical work during the third and fourth years of their course. The rates are very cheap at this school, as I was informed that a student could get his veterinary education and living on the payment of something like 450 francs ($90.00) per year. There is a dormitory for the students upon the grounds.

On a second visit to the school I met a Chinese student, who informed me that his government sent him there and paid his expenses and that when he returned he would be the first veterinarian in China.

I was informed that the Alfort school is supported by the government under the Secretary of Agriculture and gets an annual appropriation of $175,000.

As in Germany, military service is also compulsory in France, but apparently no allowance is made for the veterinary education, as I was told that the veterinarian must spend two years in the army either as an army veterinarian or common soldier.

The veterinary school at Brussels, Belgium, under the directorship of Professor DeGive, is evidently an old school, and there is a larger proportion of old buildings here, with perhaps the exception of Zürich, than the other schools visited. I was informed that the course in this school is six years in length, the first two years being taken in the university, and that such subjects as botany, physics, zoology and psychology are taken there and the remaining four years are spent in the veterinary school. Or if the four years in the veterinary school are regarded as the period of professional work, then it may be accepted that the two years of university work are required for entrance to the veterinary school.

The tuition is 300 francs ($60.00) per year, with an additional charge of 20 to 60 francs ($4-$12) for laboratory fees. There are 150 students in attendance. It is entirely optional whether the student shall go into the army or not, as veterinary military service is not compulsory in Belgium.

One of the facts, I think, which impresses the American visitor to the veterinary schools on the continent is their extensiveness, the grounds are spacious and there are numerous buildings upon them, a single building for one or two departments, with their laboratories

and museums, being larger than the whole equipment in some of the American schools.

Governmental support of schools as it exists in Germany is conducive to a high degree of efficiency. Some of the advantages are: uniformity of entrance requirements; none but well educated and qualified veterinarians are in practice. An illegal practitioner is, I judge, a *rara avis* in that country. With practically the same regulations, the system of instruction is interchangeable and a student may transfer from one college to another without loss of time or credit. In some instances living quarters are given to the teachers in addition to their salaries.

The methods of instruction of the German schools I visited while in session, attending lectures, clinics, etc., are, I understand, typical of the others. According to the schedule some of the work begins at seven o'clock in the morning and some continues until six P. M. In none of the lectures which I attended, although present promptly on the hour, did any of the lecturers begin until from fifteen to twenty-five minutes after the hour had struck. This long delay is customary throughout Germany in other branches as well as the veterinary.

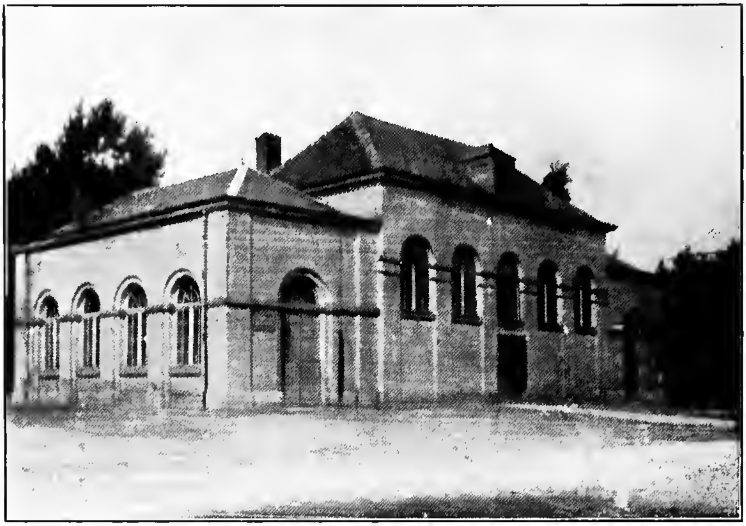
There is not, as I observed it, the paternal interest in the student as in America. The German system of having the chief examinations at the end of the course—apparently on the plan of "pay when you get through"—results in quite a large percentage of students not getting through at the scheduled time, because of dilatoriness and not keeping up to the mark. This again is a custom which is prevalent in Germany in the universities as well as veterinary schools.

Although the schools are well provided with laboratories, and they are finely equipped, and although they are used for research by assistants or advanced students, the idea was impressed upon me that the laboratory courses for the *undergraduate* students could stand a higher degree of development in such branches, for example, as physiology, pathology and bacteriology.

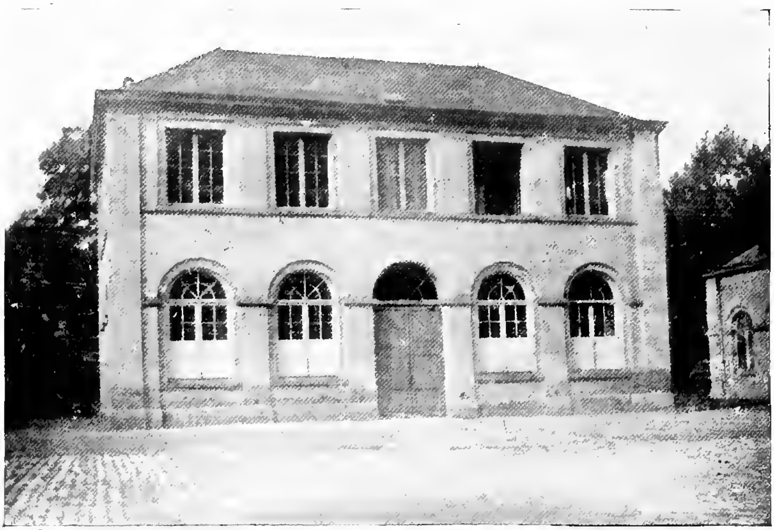
In France, although the government is generous in its appropriation to the Alfort school, the conditions surrounding the veterinarians in practice are not of the most desirable. I was informed that practice in veterinary medicine was practically open to anyone who wished to take it up. Veterinarians from other countries may

Clinical Area, Alfort, with a view of Statue of Bourgelat in the distance

Entrance to the Alfort School, with Administration Building in the distance.



Clinical Building, Brussels.



Building for Veterinary Anatomy, Brussels.

settle in France without let or hindrance, which is no disadvantage if they are properly qualified. But the absence of legal restrictions, except in connection with outbreaks of contagious or infectious diseases, against unqualified persons taking up the practice of veterinary medicine is a condition which can have no other effect than to retard veterinary progress in that country.

The veterinary schools in Holland and Switzerland appear to follow more or less closely the methods of Germany; while the school in Belgium is apparently more like those in France.

The European schools have the prestige of age. The first veterinary school was founded at Lyons, France, in 1762. Other schools were established soon afterwards; one appeared at Alfort in 1765; others at Copenhagen in 1773; at Dresden in 1774; at Vienna in 1777; at Hanover in 1778; at Buda Pest in 1786; at Berlin and Munich in 1790; at London and Milan in 1791 and at Madrid in 1793.

Although earlier attempts may have occurred, the first successful establishment of a veterinary school in America was that of the New York College of Veterinary Surgeons, which was chartered in 1857. The Ontario Veterinary College at Toronto, Canada, was established in 1862, and the American Veterinary College in 1875. Since then others have been established, some of them with state support, but the proportion of the number of veterinary schools to that of the general population is still apparently less in America as compared with Europe. Relatively, veterinary science is young in this country, and the prestige of years and adequate financial and government support is still to be attained.

Presented at the 44th annual meeting of the American Veterinary Medical Association, Kansas City, Mo., Sept. 10-13, 1907.

TETANUS.

D. K. EASTMAN AND G. R. CHASE.

The synonyms of tetanus are lockjaw and trismus. It is an infectious disease of man and animals in which the specific organisms are localized at the place of inoculation. The disease is characterized by tonic spasms of the voluntary muscles in a given region, or more commonly it affects all the skeletal muscles. It is the result of a specific wound infection.

In addition to man it occurs frequently in horses, asses and mules, and next to them are small ruminants, such as the sheep and goat. It occurs least often in the dog, and very rarely in birds and fowls.

Tetanus is one of the old diseases that was recongnized and described before the Christian era. Though it was not clearly differentiated until the discovery of its specific germ in 1884.

The cause of the disease is a slender bacillus 2 to 5 microns in length. It forms spores which are at the end of the organism, giving it somewhat the appearance of a pin. It has the distinction of producing the most powerful poisonous toxin of any of the known bacteria.

The shortest period of incubation which seems to be reported is a few hours, and the longest six weeks. In horses the period of incubation is from four to twenty days, but inoculating with the pure culture it is from four to five days. In sheep it is from two to four days. In guinea pigs inoculated with the infected soil the incubation period is usually not over forty-eight hours and sometimes less.

The common methods of infection are by pricks and nail punctures, in which cases the virus can be carried well into the living tissue and there is little or no bleeding to wash it out. It has been stated that the shorter the period of incubation the more severe the disease, the mortality being more than 90 per cent.

The presence of tetanus toxin in the living body causes no symptoms until it has been absorbed by the peripheral termination of the motor nerves and has passed along their axis cylinders and has reached the motor cells in the spinal cord. While the toxin is in the nerves

or spinal cells it apparently remains isolated or unaffected by any therapeutic agent which may be present in the circulating blood or lymph. The chief therapeutic effort is to prevent further absorption of the toxin and antagonize or neutralize that already absorbed. The time required for the toxin to be absorbed and to pass through the nerve represents a large portion of the period of incubation.

In the way of treatment serum antitoxin, even in quite large amounts, has not proven very satisfactory as a cure. Borrel, without appreciable success, has employed the intracerebral method of administering tetanus antitoxin upon experimental animals. The lumbar injection of magnesium sulphate, as reported by S. P. Meltzer, has proved beneficial by relieving the spasms. Bacelli's carbolic acid method, in which one dram doses for the horse, in 5 per cent. solution, administered hypodermically, has been quite favorably reported for the domestic animals. The injection may be made every two hours during the first 24 to 36 hours, and less frequently afterward.

Chloral hydrate is widely used for tetanus and is often combined with carbolic acid, especially in rectal injections. Gelsemium and various other drugs have also been recommended with variable success.

Experimental. The first subject experimented upon was a black mare weighing about 1000 lbs. She was twenty years old, but in good condition. She was inoculated in the gluteal region by making an incision through the skin and working a pocket under it with the handle of the knife. A piece of agar culture of tetanus was placed in the pocket and the wound left to heal by itself, which it did apparently by first intention.

The first symptoms were noted eleven days after the inoculation. They consisted of increased respiration, and pulse and restlessness and protrusion of the membrana nictitans. Circumstances arose which prevented the continuation of the experiment as planned. One dram of dilute hydrocyanic acid was injected intravenously, and although it produced profound results the animal did not die. On a succeeding day another dram of the acid was administered hypodermically and an ounce of carbolic acid and chloral were injected into the rectum. There was no improvement of the symptoms and upon the following day she received three separate one dram doses of hydrocyanic acid, one intravenously and the other two hypodermically. As the symptoms increased, instead of decreasing, she was given a three dram dose

of the hydrocyanic acid intravenously and a few minutes later died.

The second experiment was performed upon a spayed bitch. She was about six months of age and in fine condition. The inoculation was made by making a small pocket in the skin in the gluteal region and introducing therein a small piece of an agar culture of tetanus. As no symptoms appeared after an interval of one month the bitch was reinoculated by making a small incision in the pad of the left hind foot and placing a piece of agar culture in the incision. Again there was no effect from the inoculation within a period of one month. A third inoculation was made by preparing an emulsion by triturating a piece of agar culture of tetanus about the size of a pea in two drams of sterile water. This was injected into the peritoneal cavity with antiseptic precautions. In one week the first symptoms of tetanus, in a very mild form, were observed. The neck was somewhat stiff. There was a slight erection of the ears, and wrinkles in the skin of the forehead. The membrana nictitans was protruded and extended half way across the eyes. The eyes were dull and showed an anxious expression. The appetite was good and the temperature was 103 degrees F.

On the day before the inoculation the bitch received one dram doses of the fluid extract of Rhus Tox twice during the day. The next day the doses were given three times, and this dosage was kept up until the end without other treatment.

Nine days after the inoculation the muscles of the neck seemed to be gradually increasing in stiffness; the head was extended and the eyes appeared dull, but in other respects there was no marked change. At no time was there more than a slight trismus of the masseter muscles. There was no change in the symptoms until a week later, when there was quite marked improvement. Treatment was continued for a couple of days longer, but as the bitch appeared to be in perfect health no further medicine was given.

The third experiment was performed upon a bitch which also had been previously spayed. Like the bitch in the preceding experiment, she received three inoculations and at the same intervals. One week after the last inoculation she showed the first symptoms. The ears were erect and drawn together, the skin of the forehead was drawn up in longitudinal wrinkles. The eyes were retracted and anxious; the membrana nictitans showed slightly and there was some congestion of the mucous membranes. The muscles of the neck were

rigidly contracted and the nose extended. She responded readily to calls, but on turning kept her head in a straight line with the body. The appetite was good and mastication was not markedly interfered with. The treatment, began as soon as the symptoms appeared, consisted of one-sixth grain of pilocarpine injected subcutaneously three times daily. There was profuse salivation, lasting about twenty-five minutes after each injection. The symptoms soon became more pronounced. There was gradually increasing muscular stiffness; the jaws became partially set and permitted of but slight movement, but she could still make out to eat and drink. She also responded to calls but was stiff and moved with difficulty.

Ten days after the appearance of the first symptoms the dosage was increased to four injections daily with the effect of causing the bowels to become looser. As high as one-half grain of the pilocarpine was administered at a single dose, followed by profuse salivation, retching and vomiting and watery evacuations from the bowels. The dose was again reduced to one-sixth of a grain and some one dram doses of rhus tox were also administered. This treatment was continued for a few days and quite marked improvement followed. There was relaxation of the muscles; the nictitans was not so prominent, the eyes were brighter and the wrinkles in the forehead were not so marked. The discharges from the bowels were quite free and watery. In a little less than a month from the time of the last inoculation the bitch appeared to be well and further treatment was discontinued.

Another experiment was tried upon a small black mongrel dog weighing about 18 lbs. An emulsion containing 1 cc. of the B. Tetani agar culture was inoculated into the peritoneal cavity. The symptoms appeared within four days and were well advanced. The pilocarpine treatment was attempted, but the disease advanced so quickly that treatment was given up and the animal chloroformed. The post-mortem showed that the stomach and intestines were normal. The spleen and kidneys were congested and the liver engorged with dark frothy blood. There were petechiae and some congestion in the heart. The sublumbar muscles were rigid and engorged with blood, and there was also some congestion in the meninges of the brain.

A black gelding ten years old, suffering from tetanus, was brought to the clinic. The case was in charge of the professor of medicine, and the treatment recommended by him was the injection, per rectum, of

from one-half to one ounce each of carbolic and chloral dissolved in a quart of water. As a portion of the treatment two-dram doses of 1½ per cent. solution of eosin were injected subcutaneously. The patient recovered in due course of time.

The principal object of the experiments was to test the effect of eliminative treatment in retarding or checking the course of the disease. Rhus Tox and pilocarpine are both efficient agents for this purpose. The dog which received rhus tox from the time of the inoculation developed a comparatively mild case of the disease as compared with the dog which received the pilocarpine treatment after the symptoms had developed. The condition of the second dog became rather serious at one time, and some rhus tox was given along with the pilocarpine treatment. It is quite likely that the combined treatment pulled him through. Both dogs made good recoveries, the rhus dog recovering first and showing less marked symptoms throughout the course of the disease. Other experiments are, of course, necessary, but this preliminary work leads us to think that both rhus tox and pilocarpine are useful in tetanus largely from the eliminative standpoint.

EXPERIMENTS WITH BARIUM CHLORIDE.

W. E. FRINK AND H. B. TILLOU.

Some unpleasant results have occurred from the use of barium chloride, but, on the other hand, there have also been so many more that were favorable and this, combined with the cheapness of the drug, led us to undertake the investigation. It is not unlikely that some of the unpleasant results may have been due to impurities. In the following experiments Merck's preparations of barium chloride "highest purity" were employed. The cost was less than forty cents per pound, and there were no effects which we could trace to the presence of any impurity.

So far as we can find Percival, in March, 1816, was the first to use the drug therapeutically. He used it in glanders and in one of the cases noticed that there was purging. Labori and others noticed its stimulating effect upon the heart from experiments upon rabbits. Dieckerhoff in 1895 recommended the drug for its purgative effect, and he also used it in a number of cases of colic. The drug was administered intravenously and by mouth, either method producing purging. He noted increased peristalsis and fluidity of the feces. The cow was found to be less susceptible to barium chloride than the horse, and the sheep still less than the cow.

The following statistics are interesting concerning the use of the drug. Dieckerhoff published the observations on fifty-one cases in 1895. A few months later Brass published the results of 136 observations, out of which twelve animals died, about 9 per cent., as follows: seven with torsion of the large intestine, two of the small intestines, one with hernia through the foramen of Winslow, and one with entero-peritonitis. The doses used by Dieckherhoff and Brass varied from .25 to 1.25 grams. The drug was considered more energetic and more rapid than eserine, pilocarpine or arecoline. It was recommended that the dose be proportioned to the size of the patient, viz., .3 to .6 gram (5 to 10 grains) for small, .5 to .9 gram (8 to 14 grains) for medium, and .8 to 1.2 grams (12 to 18 grains) for large horses.

Dahlenburg used it in 32 cases without accident; Grüner in 48,

in doses of .75 to 1. gram (12 to 15 grains). In certain cases he injected two and three grams without ill results, except that the symptoms produced were intensified.

Hutyra at Buda Pest in 1897 used it in .5 to 1.2 grams (8 to 18 grains) in 191 cases without a death. Grüner, Plattner and Dahlenburg point out that fatal accidents arise from the action on the heart of large doses in concentrated form. Arriving at the coronary arteries, tetanic spasms of the muscle fibers may result and cause almost instant death.

The statistics of a number of published cases show that where death has taken place the attack of colic has lasted for some time, that there was acute derangement of the circulatory system, that the pulse was very quick and feeble, and that the systole was weak. In some cases the patient suffered from old standing heart disease. In all such cases small doses are indicated.

M. Cadiot is reported as treating his clinical cases of colic with barium chloride, using a solution of 1 to 30 in two or three injections with intervals of 20 to 30 minutes. In small doses it is still active, prompt in its action and harmless. Brass and Witt at the Berlin school have given three thousand doses without a fatal result. M. Chryet, of the Paris General Omnibus Company, has treated 445 cases with .4 gram (6 grains) doses at intervals of 15 to 30 minutes.

Dr. J. C. Callender (American Veterinary Review) considers barium chloride superior to eserine in the majority of cases. He has used it intravenously in 10 grain does for all cases of colic from indigestion. In some instances the dose was repeated in a half an hour with good results. In ordinary cases evacuation of the bowels in five minutes, with perhaps ten or more in the next half hour. He cautions against its use if there is much hyperthermia or if the pulse is not strong.

Dr. Muir, of the University of Pennsylvania, reports the following observations on the action of barium chloride:

Case No.	Dose.	Time to 1st Symptom.	No. of Defecatio		Weight of Feces.
1	15.4 grains	8 min.	7.		20 lbs.
2	30.8 grains	1 min.	24.		37¾ lbs.
3	15.4 grains	3 min.	5.		14½ lbs.
4	30.8 grains	1 min.	42.	urine passed 14 times.	26 lbs.
5	30.8 grains	9 min.	20.		Died.

No dangerous symptoms were shown at any time either of the first four cases. In the fifth or last experiment the animal was a fair sized bay gelding in good condition, pulse 50, full and strong, respiration 12, temperature 99 degrees F.

Fifteen and four-tenths grains of barium chloride were injected in the jugular at 11:00 A. M.; at 11:31 the feces had passed 11 times. At this time the pulse was full and strong at 48; at 12:07 he had defecated 18 times; watery mucus was being discharged from the anus. In order to determine the toxic dose of the drug, 15.4 grains more of the salt was injected in the jugular at 1.43; at 1.49 there was spasmodic contraction of the muscles; he fell, breathing with difficulty, and the heart ceased to beat at 1:52.

The autopsy revealed: the blood cyanosed, right heart empty, left side full; lungs normal; contents of cecum fluid; intestines distended with gas; little feces; double colon congested; small intestine normal; cause of death, heart failure.

The prominent symptoms were extreme purgation, voiding of watery mucus, only slight pain until the second dose was given, when all the symptoms of asphyxia prevailed, ending in the death of the animal nine minutes after the second dose had been given.

Dr. Muir's conclusions are as follows:

1. Barium chloride in doses of 15.4 grains may be safely administered intravenously.

2. It is a prompt and efficient cathartic in doses of from one to two grams.

3. Its administration is not followed by any severe pain or annoyance to the animal.

4. It acts quickly if there is no mechanical obstruction to the bowel, such as a calculus or volvulus; in the latter case it may cause it to untwist.

5. It has the advantage of being cheap.

6. In doses of 1 gram (15 grains) it causes no pain, while if 2 grams be administered intravenously there is some evidence of pain and distress.

7. It causes little if any swelling and no reduction in temperature.

8. Although the number of defecations may be small, the average amount of feces passed is large.

In 1898-9 Dr. C. R. Perkins used the drug experimentally upon some of the domestic animals. On a number of cases he used it subcutaneously in 10 grain doses and obtained evacuations in from three to five minutes and continued at rather frequent intervals for thirty or forty minutes. This method, however, caused, some abdominal pain, manifested by the usual symptoms of pawing, uneasiness and rolling. The symptoms persisted for two or three hours; the pulse and temperature remained normal, but the respirations were increased slightly. In some cases the salt was dissolved in distilled water and in others in normal salt solution, but no noteworthy differences were shown in the results. The intravenous injections caused the animal less discomfort.

Four cows were also utilized in the experiments. The salt was injected subcutaneously, but the usual dose for the horse produced no result. He found that from 30 to 35 grains hypodermically were required to produce an effect and then it was longer delayed and not so marked as in the horse with a smaller dosage.

When the salt was injected subcutaneously without rendering the skin antiseptic there was usually some local irritation and swelling, but this disappeared after a few days without special treatment.

The dosage recommended by Dr. Perkins for the horse is 10 grains intravenously for a thousand-pound animal and an additional grain for each additional one hundred pounds in weight.

In our own work forty-one experiments were tried, the majority of which were upon horses, the remaining number consisted of a few cows and dogs. The salt was administered intravenously, subcutaneously, intratracheally, and also in the form of a bolus and drench. The most of the experiments were confined to animals which were soon to be utilized for anatomical purposes, but in a number of cases the drug was also used upon patients in the clinic.

The following examples are taken from each of the different ways in which the medicine was administered to illustrate the symptoms, which may be considered fairly typical of each method.

Experiment No. 2. Intravenous method. The subject was an aged bay mare, showing lordosis, but appearing healthy and in fair condition. Her weight was 950 lbs.; pulse 35, and respirations 12 per minute; temperature 99.8 degrees.

Fifteen grains of barium chloride, dissolved in 10 cc. of sterile

water, were injected into the jugular vein. Champing of the jaws was noticed at once and this continued for about five minutes. The tail was at once raised and there was a passage of a little gas. The first feces, slightly moist, were passed two minutes after the injection. There were slight symptoms of colic and there were more and moister feces one minute later. There was another discharge of feces and liquid two minutes later and some liquid feces and gas within another minute. Still another passage of feces occurred one minute after this.

At this time, ten minutes after the injection, the respirations were reduced to six per minute, the pulse was 35 and the temperature 100°. There was excessive rumbling of the bowels. A number of evacuations of soft feces and liquid occurred at intervals from two to six minutes for a period of thirty minutes from the time of the injection. After this period the mare appeared normal and began eating. The first feces occurred within two minutes, and there were ten evacuations within the thirty-minute period.

Experiment No. 12. Hypodermic method. The subject of this experiment was an aged gray gelding in poor condition, weighing about 950 lbs. The pulse was 48 and weak. The respirations were 16 per minute.

Ten grains of barium chloride were dissolved in 10 cc. of sterile water and injected hypodermically, while warm, into the cervical region. No antiseptic precautions were taken. The animal soon began to shake its head vigorously and at the same time to champ his jaws.

The first feces were passed twelve minutes after the injection and consisted of a large amount of hard dry pellets. Four minutes later there was another passage of somewhat softer feces, and six minutes after this another passage of quite soft feces. During this time the animal showed some signs of pain by switching the tail, pawing, etc., but these were not so violent as in some other cases injected in the same manner. The animal soon appeared normal. The pulse was now 36 and strong and full. The respirations were 14 per minute. The first feces occurred in 12 minutes, and there were three evacuations within 25 minutes.

Experiment No. 7. Bolus. An aged black horse. The weight was estimated at 1050. The animal appeared to be healthy and in good condition. The pulse was 30 and the respirations were 16 per

minute. A gelatin capsule containing 2 drams of barium chloride was crushed in the animal's mouth. As it was believed that he swallowed none of the material another capsule containing the same amount was administered.

During the action of the drug there was no uneasiness or symptoms of pain. The first evacuation occurred in twenty minutes. The first feces were dry and firm, but later they became quite soft. The animal was observed for two hours, and during that time there occurred 24 evacuations. This number is higher than the average, as in a similar experiment upon another animal there was only one evacuation in an hour. Some flatus was passed at intervals, but no signs of discomfort were shown at any time. One hour after the injection the pulse was 28. The total amount of feces passed was very large, but the animal did not appear weakened.

Experiment No. 22. Drench. A drench consisting of a solution of 2 drams of barium chloride in a quart of water was administered. The first feces were passed 25 minutes later and were dry and hard; a similar evacuation followed five minutes later. The next feces were passed five minutes later and were softer and moist on the surface. The animal appeared to be in no pain, and at the end of the next twenty-five minutes soft feces were passed, followed by evacuations of soft feces and some fluid at intervals of 10, 10 and 15 minutes. The animal was not observed during the next hour; during that time there had evidently been one or two passages of soft feces. The animal showed no uneasiness at any time. There was no shaking of the head and champing of the jaws as when the drug was given intravenously to the same animal some time previously.

Experiment No. 30. Intratracheal method. The subject experimented upon was an old brown mare, weighing 1100 lbs., and she appeared to be in good condition. The pulse was 40 and the respirations were 14 per minute. A solution of 15 grains of barium chloride in 10 cc. of water was injected into the trachea, the needle being inserted between the rings of the cartilages. Masticatory movements of the jaws were noticed after several minutes. Fourteen minutes after injection there was a discharge of the urine. The pulse was now 34 and the respirations 12 per minute. Twenty-five minutes later more urine was passed and the groom observed that the animal urinated several times during the next hour. This method was tried

upon three horses, one of which received 30 grains intratracheally. None of the horses were purged by this method, although observed from 40 minutes to 1¾ hours. The above horse was the only one observed by this method which showed any diuretic effect.

In another experiment (No. 19) a combination of 10 grains of barium chloride and one-half grain of arecoline hydrobromide dissolved in 10 cc. of distilled water was injected into the jugular vein. The mare had a large evacuation of feces one minute later and began to champ the jaws and kept this up for about three minutes. There were seven evacuations within thirty-two minutes. The pulse before the injection was 36 and full and strong. After eight minutes it had increased to 52, but after thirty-two minutes it had fallen to 30 and was full and strong. Except for the champing of the jaws there was no evidence of pain or uneasiness.

Another combination (Expt. No. 20), consisting of 10 grains barium chloride, one-half grain escrine and 1 grain of pilocarpine was injected intravenously. A large evacuation occurred within five minutes, and there was a total of five evacuations within thirty-five minutes. As in the previous instance, there was champing of the jaws, but no other evidence of pain. Before the injection the pulse was 36 per minute and small. Thirty-five minutes after the injection it was 30 and fuller and stronger.

The results obtained by the combinations were apparently in no way especially superior to the barium chloride when used alone by the same method.

Some interesting results were obtained upon a patient convalescing from an attack of tetanus. It was noticed one forenoon that the horse was in considerable pain and a diagnosis of spasmodic colic was made. An anodyne drench was administered without apparent benefit. Three hours later an intravenous injection of 15 grains of barium chloride in sterile water were given. In about two minutes there was a large evacuation of feces, and this was followed by several more. The colicy symptoms were increased after the injection, and to relieve these 2 grains of morphine were injected subcutaneously, and this soon quieted the animal. [The colicy symptoms seemed to aggravate the tetanus, but the morphine apparently antidoted the effects of the barium chloride quite promptly.]

Experiments 26 and 27 were performed upon the same animal at different intervals. The subject was an old buckskin gelding, weighing about 1050 pounds, and was in poor condition. The animal had been given a half ounce of powdered nux vomica and an hour later began to show symptoms of poisoning. An ounce of Lugol's Solution was administered and about two ounces of chloroform were inhaled without benefit. The pulse rose to 104 and the respiration to 54 per minute and were very labored. The animal had fallen and could not arise. His recovery was considered hopeless, and as an experiment he was given 15 grains of barium chloride subcutaneously two hours after the nux had been taken. Within seven minutes the pulse was reduced to 84 and was stronger and not so intermittent. In another seven minutes it was reduced to 72, and still another seven minutes to 60. One hour later it was 50 per minute and regular and strong. Fifteen minutes after the administration of the barium the respirations were reduced to 42; they were deeper and not so labored. One hour and a half after the barium, they were reduced to 28 and appeared quite normal. At this time the animal was found on his feet, eating hay, and three evacuations of feces were found in the stall.

Two days later the same horse received a half ounce of powdered nux vomica. Toxic symptoms were shown in about one-half hour. There were muscular spasms, twitching of the eyes and jerking of the leg muscles. Slight sounds and the presence of persons in the stall made these symptoms worse. There was also profuse sweating. The respirations were 72 per minute, and very labored. The pulse was 60 per minute.

An hour and a half after the nux was given, 15 grains of barium chloride dissolved in 10 cc. of distilled water were administered intravenously. There were five evacuations of the bowels within a half an hour, the first one occurring three minutes after the injection. Ten minutes after injection the drug began to affect the respiration, reducing it from 72 to 60 per minute. After 15 minutes the muscles had begun to relax and had stopped the violent twitching; the breathing was much more regular and less labored. After 20 minutes the animal ceased sweating and the eyes ceased to roll. After 30 minutes the pulse was 60 and the respirations 25 per minute and apparently unlabored. The muscles had completely relaxed; the general appearance was much improved; a pail of water was taken and some hay was

eaten. After an hour and a quarter the pulse was 55 and the respirations were 23.

It would seem from these two experiments that barium chloride had quite a direct action in antagonizing the action of strychnine. At any rate, it shows very clearly the action of the drug on both the heart beats and respirations, in decreasing the number of each per minute and making the respirations deeper and the pulse stronger.

In one experiment (33) the animal was killed within an hour after the intravenous injection of 18 grains of the chloride. When the abdominal cavity was opened and the intestines exposed the peristaltic movement was plainly seen, and when a portion of the intestinal wall was removed for sectioning the persistent contraction of the circular muscle fibers caused the tissue to curl up so that it was necessary to pin it to a piece of cork in order to keep it flat for fixing.

Seven grains of barium chloride were given in a drench to a yellow bitch weighing about 20 pounds (experiment 36.) Feces and urine were passed soon afterward. The dose was evidently too large. There were marked colicy pains and attempts at vomiting. Vomiting did occur later and nausea was severe. As a mixture containing bismuth, carbolic acid and hydrocyanic acid did not relieve the nausea, one grain of morphine sulphate subcutaneously was admistered. This produced a sedative effect and in a short time the bitch was apparently all right.

[In some ways morphine seems to have an antidotal effect to barium chloride.]

In another experiment (No. 37) 3 grains of the chloride dissolved in a half ounce of water was given to a dog by the mouth. Two copious evacuations occurred, one in the forenoon and one in the afternoon. The animal showed no signs of pain or nausea, and the mild purgative effect of the drug was in this case highly satisfactory.

In an experiment (No. 38) one-half grain of the chloride was administered intravenously to a bitch weighing about 25 pounds. The dose was repeated a little later and she died almost immediately.

The abdominal and thoracic cavities were opened at once and the heart was found to be still beating and continued to beat several minutes. The intestines were also noticed to be twitching and jerking. From the fact that in this case the heart continued to beat after the respiration had ceased, it would appear that the animal died from

paralysis of respiration rather than from cardiac paralysis. There was no evidence of coagulation of the blood, as has been reported by some experimenters.

Throughout the experiments it was noticed that, although the feces first passed were relatively dry, those passed subsequently gradually became more moist, and the last ones were usually of a fluid character. The vigor of the peristaltic action was no doubt an important factor in hastening the evacuation of the bowels, and may, to some extent, have interfered with the absorption of the fluid from the feces as they were hurried along and thus increase the fluidity of the later discharges. It was a question if the increased peristalsis would adequately explain the increased amount of fluid in the later discharges and if the drug itself might not have a direct action upon the intestinal glands and thus increase the amount of the secretion. The following experiments were performed in order to get further light upon this point.

Experiment 39. The subject was a collie dog weighing about 40 pounds. The animal was put under complete anesthesia and an incision was made through the abdominal wall, through which a portion of the small intestine about 15 inches in length was carefully withdrawn. The contents of the intestine were carefully pressed toward either side and a ligature applied at each end sufficiently tight to exclude the passage of fluid through the lumen of the gut. Two other ligatures were applied to this isolated portion, dividing it into three sections as nearly equal in length as possible. The loops were then marked for identification by tying pieces of string loosely around them A solution of barium chloride, one grain to 1 cc. of sterile water, was injected into the intestine in loop No. 1. Two cubic centimeters of a similar solution were similarly placed in loop No. 2. The middle loop was left as a control and 1 cc. of water was injected in this. The intestine was replaced within the abdominal cavity and the opening closed. Later enough chloroform was administered to stop the heart. The ligated portion was removed from the rest of the intestines. It was at once evident that loop No. 1 was more distended than the control loop and that loop No. 2 was still more distended, its surface being smooth and shiny, while the control loop was collapsed and its surface corrugated. The control loop was found to contain a small amount of ingesta slightly moist. Loop No. 1 contained some ingesta

and more fluid, and loop No. 2, which had received 2 grains of the salt, contained only fluid in which particles of ingesta were floating. It was clear that the fluid contents of the intestines had been increased by the action of the salt. The intestinal mucosa appeared quite normal; loop No. 2 was perhaps slightly hyperemic and there was slight congestion at the points where the ligatures had been applied.

Experiment No. 40 was similar to the preceding and similar results were obtained. In Experiment No. 41 the subject was a Jersey cow. The procedure was the same as in the two cases just described. Although the cow died from an overdose of chloroform 20 minutes after the injection had been made, the intestinal loops into which the barium chloride had been injected contained a larger amount of the fluid than the controls.

Some blood pressure experiments were tried upon the horse to determine the effect of barium chloride upon the heart and circulation. The results showed a marked slowing of the heart beat, with additional force. The blood pressure also rose considerably.

SUMMARY.

The results of the preceding experiments we believe justify the following conclusions:

I. The drug in the doses recommended acts as a purgative, in degrees according to dosage, producing evacuations varying from mild catharsis to drastic purgation. This is produced by increased peristaltic movement and increased intestinal secretion. Furthermore the drug acts as a cardiac stimulant and tonic, lessening the number of and increasing the force of the beats, and raising blood pressure. The respirations are also reduced in number, but are deeper and more forcible.

We agree with Bartholow that toxic doses when given in proper dilutions 1:20 kill not by coagulation of the blood, or cardiac paralysis, but by respiratory paralysis.

II. That while the intravenous injection is a little more difficult than sub-cutaneous injection, it is more satisfactory, producing quicker results and followed by no greater irritation or other evil results, and can be given without fear of coagulation of blood or cardiac paralysis. The time after injection by this method to the first

passage feces being in most cases from 2-5 minutes, the longest interval being ten minutes. Symptoms of severe pain were not shown in any case and the effect of the drug passed in from thirty minutes to two hours, but usually in less than one hour.

III. When given subcutaneously there was some irritation at the point of injection, also more pronounced symptoms of pain. The effect was not seen as quickly, neither did the animal purge as freely.

IV. When given by mouth the effect was noted in from twenty minutes to fifty minutes. The animal purged more freely when given in a drench than when administered in a capsule.

V. The intratracheal method is unsatisfactory, producing no purgation even when given in doses of thirty grains, but the usual effect on circulation was noted.

VI. The dose given intravenously for purgative effects should be fifteen grains for a 1000-lb. horse, and one additional grain for each 100 lbs. additional. The dose given in the same manner for a cardiac tonic should be five to ten grains, according to the needs of that organ.

VII. The subcutaneous and intratracheal methods are unsatisfactory in doses that could be given with safety.

VIII. The dose of the drug when by the mouth should be two drams for a 1000-lb. horse and 15 grains should be added to this for each additional hundred pounds weight.

IX. From the few experiments on cattle it would appear that the dosage in these animals must be larger than for a horse of the same weight. We would recommend 30 grains intravenously as the minimum dose for a 1000-lb. cow for mild purgative action.

X. In dogs the dose must necessarily be small, one to four grains may be given by the mouth, according to the size of the animal, or severe nausea will follow.

The following tables show some of the more essential results in very concise form:

TABLE No. 1.

Case No	Wt.	Method of Administr'n	Dose.	Pulse Before	Pulse After.	Time to first Evac'n	No. of Evacu-ations.	Time obser-ved.	Symptoms of Pain.
I	900	Intravenous	10 grains	40	36	4 min	6	48 min	Slight.
II	950	"	15 grains	35	35	2 min	10	30 min	Slight.
III	900	"	15 grains	33	40	2 min	17	48 min	Slight.
IV	1250	"	14 grains	38	50	13 min	2	45 min	Colic.
V	1000	"	20 grains	34	30	2 min	18	32 min	None.
VI	900	Bolus	2 drams	30	24	15 min	6	1 hr.	None.
VII	1050	"	2.5 drams	30	28	20 min	24	2 hrs.	None.
VIII	1000	Hypoderm.	20 grains	42	40	17 min	2	2 hrs.	None.
IX	800	"	20 grains	40	48	15 min	2	1 hr.	Sev're col.
X	1000	Intravenous	15 grains	×	×	3 min	8	33 min	None.
XI	1100	Hypoderm.	18 grains	50	43	10 min	5	30 min	None.
XII	950	"	10 grains	48	36	12 min	3	25 min	Slight.
XIII	1000	"	10 grains	50	48	25 min	2	37 min	Severe.
XIV	1000	Intravenous	17 grains	56	48	2 min	6	25 min	Slight.
XV	850	Bolus	$2\frac{2}{8}$ drams	42	37	25 min	1	1 hr.	Slight.
XVI	850	Intravenous	$7\frac{1}{2}$ grains	40	38	40 min	1	1 hr.	Slight.
XVII	850	"	15 grains	41	38	2 min	12	42 min	Slight.
XVIII	1150	"	15 grains	×	×	2 min	(?)	×	Colic.
XIX	900	"	$\frac{1}{2}$ gr. ARECOLINE 10 gr. $BaCl_2$	36	30	1 min	7	32 min	None.
XX	800	"	10 gr. $BaCl_2$ $\frac{1}{2}$ gr. ESERINE 1 gr. PILOCARP	36	30	5 min	5	35 min	None.
XXI	1100	Bolus	2 drams	×	×	50 min	7	$2\frac{1}{2}$ hrs.	None.
XXII	900	Drench	2 drams	×	×	25 min	9	$2\frac{1}{2}$ hrs.	None.
XXIII	800	Bolus	$2\frac{2}{8}$ drams	32	32	23 min	22	$1\frac{1}{2}$ hrs.	None.
XXIV	1150	Intravenous	15 grains	49	40	5 min	6	25 min	Colic.
XXV	1250	"	15 grains	76	60	1 min	8	21 min	Colic.
XXVI	1050	Hypoderm.	15 grains	104	50	×	3	$1\frac{1}{2}$ hrs.	None.
XXVII	1050	Intravenous	15 grains	60	55	3 min	5	30 min	Slight.
XXVIII	950	Intratrach'l	15 grains	×	×	none	none	$1\frac{3}{4}$ hrs.	None.
XXIX	950	"	30 grains	×	×	none	none	$1\frac{1}{2}$ hrs.	Colic.
XXX	1100	"	15 grains	40	34	none	URINE PASSED SEVERAL TIMES	40 min	None.
XXXI	950	"	15 grains	34	30	none	none	50 min	Slight.
XXXII	1200	Intravenous	15 grains	×	×	5 min	9	30 min	Colic.
XXXIII	950	"	18 grains	40	36	2 min	15	45 min	None.

FURTHER SUMMARY OF TABLE NO. 1.

Intravenous.	Amount.	Time to 1st Evacuation.	No. of Evacuations.	Time Observed.	Pulse Before.	Pulse* After.	Pain.	Respiration Before.	Respiration After.
					(Averege of 11)			(Average of 5)	
(Average of 13)	15.3 grains.	$3\frac{1}{2}$ min.	9	35 min.	45.6	42.5	Slight 6	17	11.6
Maximum.	20 grains.	13 min.	18	48 min.	76.	60.	Colic 4	26	19
Minimum.	10 grains.	1 min.	2	21 min.	33.	30.	None 3	12	6
Hypodermic.					(Average of 6)			(Average of 4)	
(Average of 6)	15.5 grains.	16 min.	3	1 hour.	55.6	44.1	Slight 1	17	14.2
Maximum.	20 grains.	25 min.	5	2 hours.	104.	50.	None 3	23	17
Minimum.	10 grains.	10 min.	2	25 min.	40.	36.	Severe 2	13	12
Bolus.					(Average of 4)			(Average of 1)	
(Average of 5)	2.3 drams.	$26\frac{3}{5}$ min.	12	1 hour 36 min.	33.5	30.2		14	12
Maximum.	2.6 drams.	50 min.	24	$2\frac{1}{2}$ hours.	42.	37.	None 3		
Minimum.	2 drams.	15 min.	1	1 hour.	30.	24.	Slight 1		
Intratracheal.					(Average of 2)			(Average of 2)	
(Average of 4)	18.7 grains.	......	..	71 min.	37.	32.	Slight 1	13	10.5
Maximum.	30 grains.	......	..	$1\frac{3}{4}$ hours.	40.	34.	Colic 1	14	12
Minimum.	15 grains.	......	..	40 min.	34.	30.	None 2	12	9
Drench. (1)	2 drams.	25 min.	9	$2\frac{1}{2}$ hours.	..	..	None		
Intravenous.	10 grs. $BaCl_2$. $\frac{1}{2}$ gr. Areco hydro.	1 min.	7	32 min.	36.	30.	None		
Intravenous.	10 grs. $BaCl_2$. $\frac{1}{2}$ gr. Eserine. 1 gr. Pilocarpine.	5 min.	5	35 min.	36.	30.	None		

*In a few cases an acceleration of the pulse was noticed as an effecf of the drug.

RHUS TOXICODENDRON.

J. N. FROST.

The principal synonyms are: Mercury, poison oak, poison or three-leaf ivy, climbing or trailing sumac.

Its trifoliate leaves serve to distinguish it from the harmless Virginia creeper, "Ampelopsis quinquefolia," with which it might otherwise be confounded.

Poison ivy is the most important cutaneous vegetable poison in existence. The popular impression that poisoning can occur without direct contact with the plant is verified and is explained on the theory that pollen grains or minute hairs loosened from the leaf are deposited upon the skin.

The tincture is the most convenient and reliable preparation and may be made from the green or freshly dried leaves. The green leaves are better, as the medicinal virtues seem to be volatile and the preparation is said to deteriorate by long keeping.

Constituents.

Tannin, wax, gum, starch and resin have been found in the drug, together with the peculiar alcohol soluble oil or fat, Toxicodendrol, closely allied to cardol.

Toxicodendrol, believed to be the active principle, is found to the extent of 3 per cent. in the leaves and is easily soluble in ether, alcohol and chloroform. It also forms an insoluble compound with lead, which fact is made use of in the treatment of poisoning.

Action.

On man the volatile acid of Rhus Tox is a powerful local irritant, producing the characteristic eruption. This eruption may spread to other parts of the body, or to another by coming in contact with the poisoned skin, or by using the same towel as a patient suffering from poisoning.

Death is not known to have occurred from poisoning with this plant. The effects pass off in a few days, but may return again the following year at the same date, and may recur in this way for several years.

The action of Rhus Tox upon the nerves is similar to that of Nux Vomica, but not so pronounced.

The herbivora devour the leaves with impunity. The juice is reported as being fatal to dogs, but this was found to be incorrect with the fluid extract.

Rhus Tox is a favorite remedy with homeopathists in all cutaneous affection of a vesicular type, and they prescribe it in the chronic forms of rheumatism, neuralgia, paralytic affections, lumbago, sciatica, incontinence of urine, stiffness from getting wet, etc.

Externally it is recommended as an application in sprains, injuries to ligaments, tendon and muscles, burns, stings of insects, chilblains, hemorrhoids, varicose veins and warts.

Cases of poisoning in the human subject from the leaves are very common and numerous remedies are in use. Those probably the most effective and also the most frequently employed are lead water and laudanum, or the fluidextract of Grindelia. The fluidextract of the plant itself is recommended for a preventive and also as a curative agent when taken internally. A remedy very frequently used is lead subacetate. An alcoholic solution is preferable to the aqueous. An alkaline treatment is also recommended. [A solution of quinine applied to the parts has also been highly recommended.]

Therapeutically it is said that the plant attracted the attention of Dupresnay in France about the close of the eighteenth century, who noticed the accidental poisoning of a student suffering from eczema, and that the eczema disappeared on the subsidence of the Rhus poisoning.

Paralysis of a rheumatic character is benefited. Dr. Phillips recommends its use both internally and externally in various subacute and chronic rheumatic affections of fibrous tissue. It has also been recommended for incontinence of the urine. Dr. B. Powell, a sufferer for years from rheumatism and hemorrhoids, found the remedy benecial in both ailments. Although he began treatment in a spirit of scepticism, he began to feel better in three days than he had for months respecting the rheumatism. As to the hemorrhoid he found himself entirely free from rectal annoyance while taking Rhus, although upon stopping it, the piles immediately returned. Dr. J. R. Taylor found its action very rapid in relieving muscular soreness. Cases of

muscular rheumatism, lumbago and torticollis have been reported as quickly relieved by the use of Rhus.

The following experiments were carried on with the purpose of determining as far as possible how valuable the drug might be in veterinary practice.

Exp. No. 1.

A puppy bitch, weighing about 15 pounds, was placed in the kennel for collecting urine. About 8 oz. was passed in 18 hours (3 p. m. to 9 a. m.). It was examined immediately afterwards. No. feces were passed during 18 hours.

URINE.

Sp. gr.	1023
Reaction	Acid
Color	Light yellow
Solids	53.59
Chlorides	7.705
Phosphates	.9191
Sulphates	2.5
Urea	28.
Albumen	None
Sugar	None
Bile	None
Hemoglobin	None

The animal was placed in the kennel for collecting urine at 3 p. m. and given four pills of one-half minim each of Rhus Tox. At the end of 18 hours 6 oz. of urine were found. The urine was examined immediately afterwards.

Sp. gr	1048.5
Reaction	Acid
Color	Yellowish red
Solids	113.005
Chlorides	6.164
Phosphates	4.3329
Sulphates	11.
Urea	39.
Albumen	None
Sugar	None
Bile	None
Haemoglobin	Present

Exp. No. 2.

A dog was chloroformed and the small intestines were drawn out through an incision on the median line of the abdomen. The ingesta was forced out of the intestine as much as possible and three loops were tied. One loop 4½ inches long was used as a check. Another loop 4½ inches long was injected with one minim of the fluidextract of Rhus Tox undiluted. Another loop 3½ inches long was injected with four minims of the Rhus Tox undiluted. The intestines were replaced and the abdomen sewed up. After one hour (the dog having been under complete chloroform anesthesia) the intestines were again drawn out.

The check loop contained nearly solid ingesta. There was no difference in the loop injected with one minim and the loop injected with four minims. Each contained a semi-solid mass, and in each there was considerable congestion of the mucous membrane.

Exp. No. 4.

A small calf weighing 75 lbs. and less than one week old, after fasting for 24 hours, was given 2 oz. of Rhus Tox, diluted with 4 oz. of water, at 8.15 a. m.

Temperature 101.9,	8:15 a. m.,	Respiration 21	Pulse 160
	8:30 a. m.,	" 26	" 120
	8:45 a. m.,	" 26	" 116
	9:00 a. m.,	" 25	" 105
	9:15 a. m.,	" 23	" 105

At 9.30 the animal was killed by bleeding, but showed no ill effects from the large dose of the drug.

Exp. No. 9.

A gray gelding weighing about 1000 pounds was given 1 oz. of the fluid extract of Rhus Tox in 4 oz. of water at 10.45 a. m.

10:45 a. m.,	Pulse 30	Respiration 10	Temperature 99.8
11:45 a. m.,	" 23	" 6	" 99.8
12:30 p. m.,	" 22	" 6	" 99.7
2:15 p. m.,	" 24	" 7	" 99.9
4:00 p. m.,	" 25	" 8	" 99.8

Exp. No. 12.

A Holstein heifer 1 year and 5 months old. She was pregnant and weighed 660 pounds. She was given 1 oz. of the fluid extract of Rhus Tox in 4 oz. of water.

2:00 p. m.,	Pulse 45	Respiration 18
3:00 p. m.,	" 45	" 17
4:00 p. m.,	" 41	" 17
5:00 p. m.,	" 40	" 16

Exp. No. 13.

A spotted gelding 12 years old, weighing 1040 pounds. Four drams of Rhus Tox were given in a bran mash in place of a feed of oats.

1:50 p. m.,	Pulse 40	Respiration 15
2:00 p, m.,	Feces were passed.	
2:50 p. m.,	Pulse 25	Respiration 8
3:00 p. m.,	Urine passed.	
3:50 p. m.,	Pulse 24	Respiration 7
4:50 p. m.,	" 32	" 10
5:50 p. m.,	" 35	" 10

Exp. No. 14.

In this experiment an attempt was made to produce the cutaneous form of poisoning in the different domestic animals.

The fluid extract was thoroughly rubbed into the muzzle and also the eyelids of a cow, but with no effect. On the horse the drug was thoroughly rubbed into the skin of the neck and lower jaw, after thoroughly shaving and washing the parts. This also failed to produce the poisoning.

On the dog the left flank and under side of the abdominal region were soaked with the drug, but we were unable to produce either an eruption or redness of the skin.

Exp. No. 17.

This experiment was started with the intention of producing poisoning in the dog if possible, but through a misunderstanding some tetanus organisms were injected into the animal.

Feb. 8. The dog was given one dram of the fluidextract of Rhus Tox in ½ oz. of water three times daily.

Feb. 9. The dog was given the same dose. On this day an emulsion was made by triturating a piece of agar culture of tetanus about the size of a pea in two drams of sterile water. This was injected into the peritoneal cavity under antiseptic precautions.

Feb. 16. The dog had been receiving one dram of fluid extract of Rhus Tox three times daily up to the present time. The first symptoms of tetanus appeared. The neck was somewhat stiffened, the ears were

semi-erect and a few slight wrinkles appeared in the forehead. The membrana nictitans was greatly protruded and extended nearly half way across the eye. The animal showed but slight stiffness in trotting about the kennel.

Feb. 17. Same treatment continued. No noticeable change.

Feb. 18. Same treatment. The muscles of the neck appeared more stiff, but the gait was improved.

Feb. 23. Treatment continued to date. The stiffness of the neck muscles and wrinkles had about disappeared, but the membrana nictitans was still protruded.

Feb. 28. The same treatment which had been continued to date was now stopped. Animal seemed in perfect health, although a little thin in flesh. At no time did the dog fail to respond when called, and was always ready for its two meals daily.

No poisoning occurred and the skin remained soft and smooth.

At the same time that the dog in the above experiment was inoculated a second dog was also inoculated with the tetanus bacillus. This second animal was treated with injections of pilocarpine and suffered much more severely than the one under treatment with Rhus Tox.

The following experiment shows the effect of the Rhus upon the metabolism of the body as determined by the examinations of the urine.

Experiment No. 18.—Human urine examined before using drug :

	1st day.	2d.	3d.	4th.	5th.	6th.	7th.	Average.
Amount	850cc.	750	775	815	865	795	765	$802\frac{1}{7}$ cc.
Sp. gr.	1026	1026	1024	1020	1024	1022	1024	$1023\frac{3}{7}$
Solids	60.50	60.58	55.92	46.60	57.	51.26	55.92	55.40
Chlorides ...	21.57	22.06	20.03	16.02	3.39	4.15	23.11	16.14
Phosphates..	3.93	1.27	1.96	1.85	.9191	1.07	1.70	1.81
Sulphates ...	2.	4.	2.	1.	2.	2.	1.	2.
Urea	27.5	22.	25.	19.	20.	21.	26.	22.84
Uric Acid	.245	.55	.218	.208	.280	.205	.231	.276

After taking one-half minim three times daily :

	1st day.	2d.	3d.	4th.	5th.	6th.	7th.	Average.
Amount	880 cc.	875	915	1045	925	1115	—	959 cc.
Sp. gr.	1026	1026	1026	1028	1030	1030	—	1027.6
Solids	60.58	60.58	60.58	65.24	69.90	69.90	—	64.46
Chlorides ...	26.19	22.05	22.07	24.32	6.16	8.04	—	18.13

Phosphates..	1.59	2.16	2.44	2.26	1.84	4.84	—	2.50
Sulphates....	2.	2.	3.	2.	1.	3.	—	2.1
Urea	28.	30.	34.	40.	40.	42.	—	35.6
Uric Acid	.245	.47	.55	.50	.653	.76	—	.52

After taking one minim three times daily :

	1st day.	2d day.	Average.
Amount......	1015 cc.	925	965 cc.
Sp. gr.	1028	1028	1028
Solids........	65.24	65.24	65.24
Chlorides	17.02	14.42	15.72
Sulphates	1.	2.	1.5
Urea..........	32.	35.	33.
Uric Acid	.44	.33	.38

After two days symptoms of poisoning appeared and the administration of the drug was stopped.

After experiment had been finished :

	2d day.	3d day.	4th day.	5th day.	Average.
Amount......	1000 cc.	880	915	825	905 cc.
Sp. gr........	1026	1024	1018	1022	1022.5
Solids........	61.58	55.92	42.94	51.26	52.67
Chloride	20.03	18.02	4.15	15.08	14.32
Sulphates	1.	2.	2.	2.	1.7
Phosphates...	2.44	1.84	3.39	.919	2.145
Urea.........	26.	26.	20.	22.	23.5
Uric Acid	.30	.28	.218	.280	.269

In conclusion let us consider first the dosage. For man the average dose is given as from ½ to 2 minims of the tincture or fluid extract three or four times a day.

For the dog the dosage may be from one to fifteen minims, depending on the size of the animal, although as high as one dram has been given three times daily without ill effects.

In the horse one or two drams seem to produce about the same effect as the ounce dose, although the action of the larger dose is naturally more prolonged.

The cow is said to devour the leaves with impunity, and in my experiments a one ounce dose seems to have very little effect.

Its good effect, especially in the case of rheumatism, would seem to be due to its eliminating properties, which is especially carried

on by the kidneys. The urinary examinations show that the drug caused an increase in the solids, particularly urea.

It should prove of benefit in diseases where recovery depends upon the eliminations of toxic properties from the body, as azoturia and similar diseases. Its good effect in the experimental case of tetanus would seem to be due to the elimination of the toxic product from the cells.

REFERENCES.

American Journal of Pharmacology, 1895.
American Journal of Medical Science, April, 1866.
Pharmaecutical Era, Dec. 6, 1906.
Medical Record.
Medical and Surgical Reporter, Nov. 2, 1867.
Indian Lancet, April 16, 1896.
Medical World, April, 1890.
Medical News, April 20, 1887; Nov. 9, 1889.
Therapeutic Gazette, Oct. 15, 1889.

TABLE OF CONTENTS

EXPERIMENTS WITH PILOCARPINE HYDROCHLORIDE

L. V. POLK

Pilocarpine is one of the alkaloids of the plant Pilocarpus of which there are several varieties. It is claimed the plant and drug were first described by Piso in 1848 and was at that time used by the natives as an antidote to certain poisons. Its pronounced virtues as a medicine were not discovered until 1873, when Contuiho of Brazil claimed remarkable diaphoretic properties for the drug and, on bringing some to Paris, had his observations corroborated by Dr. Gubber in a hospital in that city.

The alkaloid pilocarpine was discovered almost simultaneously in 1875 by Hardy in France and Gerrard in England. Drs. Weber, Bardenhewer and Auschinam agree that 3 grains of pilocarpine are equal to 75 grains of the best leaves. Pilocarpine is superior to jaborandi because of its more certain action. It is less disagreeable and less apt to cause nausea.

Besides pilocarpine, there are present in the leaflets two other alkaloids: jaborine and pilocarpidine. The action of the latter appears to be identical to that of pilocarpine while the action of jaborine is quite antagonistic. This is said to be due to a difference in the molecular arrangement as their composition appears to be very closely related. By heating in the presence of a concentrated acid solution, pilocarpine is changed to jaborine and by washing with absolute alcohol they are separated. The salts of jaborine do not crystallize while those of pilocarpine do. Salts of jaborine dissolve more easily in ether and less easily in water than do those of pilocarpine. Physiologically the difference between the two alkaloids is even more readily noticeable; jaborine acts almost exactly like atropine, to which pilocarpine is a complete physiological antagonist.

Pilocarpine hydrochloride (C_{11} H_{16} N_2 O_2 HCl) is obtained by neutralizing the pure alkaloid with diluted hydrochloric acid, concentrating the solution and crystallizing. If ignited the salt burns

completely leaving no residue. The salt is usually administered hypodermically and in my experience is, if anything, more rapid than when administered intratracheally.

Dosage. The usual doses recommended for the horse hypodermically are from 2 to 5 grains and for the dog from 1-40 to 1-6 grain. Kaufman claims that horses are poisoned by subcutaneous doses of 5 grains. Fieser claims to have injected a cow and a bull subcutaneously with from 3 to 18 grains and experienced no bad effects. Fröhner has observed a dog killed by pulmonary edema following the injection of 3-4 grain. In my work, 1-6 grain doses have given all the results that could be expected. Cats should receive a little less than half the dose for the dog. Ringer points out that the effects produced on the young are much less marked for corresponding doses than upon adults.

Antagonists and Incompatibles. The incompatibles of pilocarpine are the caustic alkalies, per salts of iron and metallic salts generally; calomel and potassium permanganate; tannic acid and alkaloidal precipitants. The antagonists are belladonna and its alkaloid atropine and stramonium. It is stated that 1-100 grain of atropine will overcome the effects of 1-6 grain of pilocarpine. Morphine overcomes the vomiting which is sometimes occasioned by the use of pilocarpine.

Synergists. Aconite, veratrum viride, gelsemium, muscarine, arecoline hydrobromide, picrotoxin, physostigmine, nicotine, apomorphine, spirits of nitrous ether, barium chloride.

Digestive System. Pilocarpine, even in very small doses, greatly increases the salivary secretion. This was demonstrated to a marked degree in my experiments. The parotid gland seems to be more forcibly stimulated than the others. In one of my experiments on the horse a cannula was inserted into the duct from the left parotid gland and the duct from the right gland was ligated. After a small hypodermic injection of pilocarpine, there was a steady flow of saliva through the cannula while the saliva in the mouth was but little if any increased in amount. Cushny and Hoare concur in the opinion that the action of the pilocarpine is on the termination of the secretory nerve endings. After the injec-

tion of small amounts of atropine, pilocarpine, in ordinary doses, produces no increase in any of the secretions. As atropine paralyzes the nerve endings, the indication is that pilocarpine is not able to overcome this paralysis and has no direct action upon the cells themselves.

Some experiments were performed to determine if pilocarpine increased or decreased the digestive action of the saliva and if it thereby affected the amount of ptyalin in the secretion. The results were rather contradictory but in the main it appeared as if the ptyalin was somewhat diminished. A possible explanation is that the amount of the fluid in the secretion was increased so much that it had the effect of diluting the ptyalin and thereby causing some diminution of its digestive action.

It has been stated by some investigators that urea was present in the increased secretion in quite notable quantities. In my experiments I have been able to demonstrate the presence of urea in small amounts after the injection of the alkaloid, but the amount has been so small that it would appear to be of but little importance in removing this waste product if the regular channel of elimination through the kidney were interfered with.

The gastric secretion is increased after the injection of pilocarpine and the movements of the stomach are also accelerated. The drug sometimes causes nausea and vomiting. Whether this is caused by the presence of an excess of fluid secreted or to abnormal movements has not been definitely decided. Small doses of morphine will usually antagonize this action.

In impaction of the omasum and rumen of cattle this drug has proved of some value. Dr. James Law mentions pilocarpine in the treatment of impaction of the omasum. He states that pilocarpine is theoretically the best agent for this trouble as its tendency to cause free secretions from the mucous surfaces and even a slight secretion from the omasal folds will greatly favor the detachment and discharge of the impacted masses. He recommends a dosage of 3 grains in this connection and the same amount for the treatment of impaction of the rumen.

The intestinal secretions are, according to most authors, rather copiously increased by the administration of pilocarpine. Cushny

states that the intestines are unusually active in movement and repeated evacuations of their contents follow. These are at first firm but as the peristalsis carries the contents of the small intestines toward the exterior, which have not had time to have the fluid absorbed, the feces contain more water than usual. While admitting that the fluidity of the stools may be in part, increased by augmented intestinal secretion, he adds that the fact has not been satisfactorily demonstrated.

In veterinary practice eserine is frequently combined with pilocarpine and there is not much doubt that this combination has a marked effect in stimulating the peristalsis of the bowels.

Circulation. On the circulation pilocarpine acts as a depressant rather than as a stimulant. There is first a temporary increase of the blood pressure and dilatation of the capillaries, then the heart is slowed and the pressure falls. The dilatation of the capillaries is more noticeable in man than in the lower animals, for even with a small does of the alkaloid in the human being there is a distinct flushing of the skin and a free secretion of sweat. The latter result I have noticed only once in the horse and that was after two injections of eserine and pilocarpine had been given for the relief of impaction.

The direct result of the relaxation of the capillaries is a diminution in the obstruction of the blood stream and therefore a fall in the blood pressure. The heart is then slowed and the beat lessened in force for the reason that not so much power is required to force the blood through the relaxed capillaries.

The elements of the blood are apparently influenced after the administration of pilocarpine. The red cells are seemingly increased in number and there is a higher percentage of hemoglobin. It has been pointed out that this may occur after the administration of most purgatives where there is an increased loss of the fluid portion of the blood through the bowel. As a result the blood becomes more concentrated and there is an apparent increase in the number of the red corpuscles and a higher percentage of hemoglobin. The leucocytosis appearing after the injection of pilocarpine may also be only apparent as in the case of the red cells, because of the more concentrated condition of the blood.

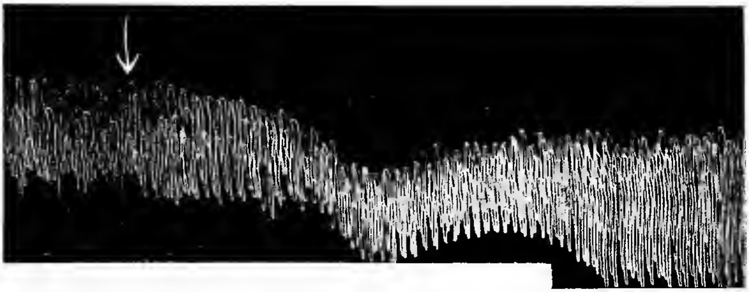


Fig. 1. Blood pressure tracing from horse (No. 70). One grain of pilocarpine was injected intravenously (0.146 mg × kg) at the point indicated by the arrow.

Reduced about 1-3.

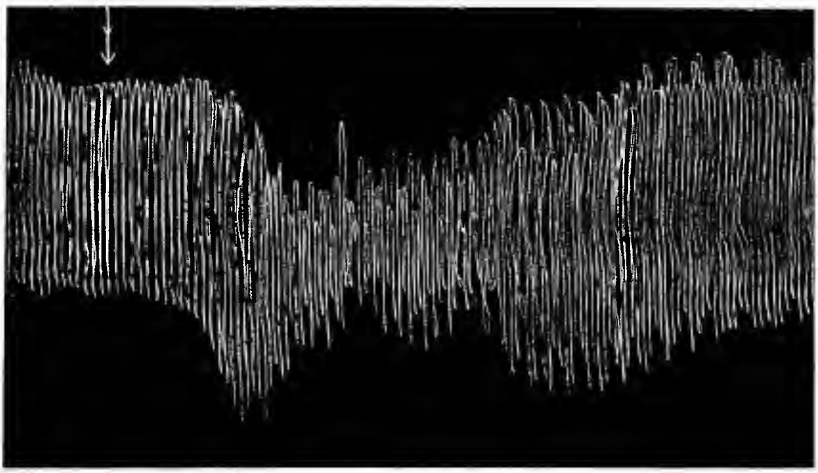


Fig. 2. Blood pressure tracing from cow (No. 39). One grain of pilocarpine hydrochloride was injected into the jugular vein at the point indicated by the arrow.

(Tracings loaned by Dr. Fish) *Reduced about 1-3.*

Observations in connection with the use of pilocarpine in infectious diseases indicate that it has an action in preventing the accumulation of toxins in the body and thus prevent paralysis of cellular activity and assisting perhaps in the formation of antitoxins. The toxilytic action of the liver is increased and the glands helped in their defensive work. Leucocytosis is also probably a factor. In this connection I quote an experiment upon two guinea pigs, which were given a lethal dose of diphtheria toxin and not quite enough antitoxin to counteract it. One guinea pig was treated with 1-30 grain doses of pilocarpine. The other was not treated. The latter died in 36 hours, while the former showed no effects whatever from the toxin.

In an experiment of my own, tetanus was induced in a bitch. She received injections of pilocarpine hydrochloride in 1-6 grain doses three times daily. A good recovery resulted. The beneficial effects may be due to the stimulating action upon the cells, increasing the secretions—a cell catharsis, by which the toxins were washed out. Leucocytosis may also be considered in this connection. The intensity and progress of the disease are also factors and unfavorable results have been obtained when the disease had gained too much headway.

In human practice pilocarpine has been recommended as a curative and preventive agent in diphtheria. It has also been recommended in scarlet fever.

Urinary Apparatus. On the kidneys especially some of the chief effects of pilocarpine are noticeable. The amount of urine varies with the dose administered. A small dose will increase the flow while a larger dose will cause diminution of the secretion. In my experiments on the human urine I have found this to be true. Waugh and Abbott have also noted this variation and claim that the desire to urinate is always very strong. A small dose present in the blood streaming through the kidney has a chance to stimulate that organ and yet is not strong enough to cause anything like a free action of the cutaneous glands. On the other hand, next to salivary increase, a large dose acts forcibly on the skin glands, driving the liquid from the body by that channel. Therefore more water is lost through the skin and less by way of the kidney under a large dose

of pilocarpine. In a number of my experiments there was a free excretion of urine but no sweating. In only one horse did I notiee any diaphoresis, and in that ease there was no urination.

It has been shown that the urinary solids are inereased. Of these the most notieeable inerease is seen in the urea. In any trouble either in the kidney or elsewhere when there is either an increased production or decreased dissipation of urea, piloearpine would be useful. In some slight or ehronic inflammation of the kidneys, sueh as "Brights Disease" and glomerular inflammation, the excreting funetions may be stimulated and small doses of this drug would be indicated. In case of a weak or fatty heart or ehronie nephritis it should be used with considerable caution.

Skin. The diaphoretie action is more markedly shown in man than the domesticated animals. With the exception of the horse, the other animals are not well provided with sweat glands. Although the horse is well provided with such glands the aetion of the drug as a diaphoretic is uneertain and unsatisfactory. Sweating occurs either as a result of the extreme dilatation of the eutaneous vessels, thereby bringing more blood to the glands, or, as a result of direet stimulation of the glands by the drug. It is not unlikely that both faetors may eontribute.

The sweat produced by pilocarpine is at first acid, then neutral, and after flowing some minutes is alkaline. Both the fluid and solids of the sweat are inereased in amount and an increased amount of urea is said to be present. In diseases of the kidney this eondition would, of eourse, be favorable.

The dilatation of the eutaneous vessels may aceount for the variations in temperature. The presence of a greater amount of blood to the surfaee would favor heat dissipation, but it is also elaimed that there is a diminution of the production of heat.

There is some evidence that pilocarpine stimulates the growth of the hair. It has been recommended in human praetiee for baldness. By inereasing the moisture of the skin and improving the eireulation and nutrition some benefit may result.

Nervous System. Moderate doses produce apparently but little effect upon the central nervous system. Large doses may produee hiceoughs, trembling and dizziness. The peripheral nervous system

is more directly affected as is evidenced by the stimulating effect upon the endings of the secretory nerves. The drug also stimulates the nerve endings in the involuntary muscles causing increased peristalsis. It also stimulates the bladder, uterus, spleen and heart.

In nearly all of my experiments there has been a certain nervousness manifested by the subjects. In the horse there has been champing of the jaws, uneasy movements, pawing, etc., and in the cat and dog by restlessness and an anxious expression.

Pilocarpine has been used with some success in certain diseases of the nervous system, principally spinal meningitis and chronic hydrocephalus. In the latter disease the alkaloid in large doses favors the reabsorption of the exudate in the ventricles. The drug is "pushed until the desired result is obtained and it is very rare that an animal is poisoned because of its rapid elimination."

Respiration. In my experiments moderate doses slightly increased the respirations. Generally the increase was only two or three per minute, but the acceleration was constant. The secretion of the bronchial mucus is increased. Fröhner observed the death of a dog from edema of the lungs after receiving 3-4 grain of pilocarpine. In increasing the bronchial secretion the drug would appear to be indicated in chronic bronchitis and has been so recommended. In coryza, bronchitis and laryngitis pilocarpine has been recommended in small doses followed by quinine and this procedure is said to be just as effective as large doses and safer.

Temperature. The physiological action of pilocarpine is to first cause a slight rise in temperature and then to distinctly lower it. In man this may be due to the dilated cutaneous vessels, but in the horse the same result occurs although, as a rule, there is no sweating. In the horse I have observed a drop of one degree in temperature following the hypodermic injection of one grain of the muriate. The normal temperature is again usually reached in from one half to one and a half hours. In the horse it may be that the drug decreases the production of heat.

Eye. The action of pilocarpine on the eye is to cause contraction of the pupil. In my experiments this was always noticed in the horse and cat, the pupil contracting to a mere slit. According to Cushny the contraction reaches a maximum in 1-2 to 1 hour and

passes off in 3 to 5 hours. It is generally less complete and of shorter duration than that seen after the administration of eserine.

Uterus. It is claimed that pilocarpine stimulates the contractions in the gravid uterus, but has little or no effect on the unimpregnated organ. Cases have been reported in human practice where its use subcutaneously has induced premature labor.

Absorption and Elimination. Absorption occurs rapidly when given either by the mouth or hypodermically. It is eliminated by the skin, kidneys, saliva, gastric and intestinal glands and bronchial mucous glands. Elimination is also claimed through the mammary gland and that it acts as a glactagogue in the cow, but satisfactory evidence is not as yet forthcoming.

EXPERIMENTAL

The following table summarizes the general effects upon seven horses and one cat:

No.	Subject	Amount	Method	Pulse Before	Pulse After	Temperature Before	Temperature After	Respiration Before	Respiration After	Defecation	Urination	Time observed
1	Black Gelding 18 yrs. 1000 lbs.	1 grain	Hypo-dermic	30	10 min. 33	100.3	10 min. 99	13	10 min 14	In 5 & 28 min.	19 min.	45 min.
2	Mare 18 yrs. 1050 lbs.	1 grain	Intra-tracheal	37	15 min. 38 20 min. 42	100.2	15 min. 100 20 min. 100	12	15 min. 14 20 min. 14	30 min.	None	60 min.
3	Mare 16 yrs. 900 lbs	1 grain	Intra-venous	30	20 min. 39 25 min. 36	100	20 min. 100 25 min. 99.4	12	20 min. 13 25 min. 14	3 & 38 min.	4 min.	50 min.
4	Black Gelding 8 yrs. 850 lbs.	1 grain	Intra-venous	50	6 min. 43	99.3	6 min. 99 16 min. 99.8	11	9 min. 13	Flatus	None	45 min.
5	Gelding 22 yrs. 900 lbs.	2 grains	Hypo-dermic	30	19 min. 42 31 min. 40	100	9 min. 99 31 min. 99.8	12	19 min. 8 35 min. 10	10 & 13 mins. watery	10 min.	45 min.
6	Gelding 20 yrs. 1200 lbs.	2 grains	Intra-venous	32	10 min. 60 15 min. 48	99	10 min. 99	13	10 min. 18 15 min. 24	15 & 25 min.	None	40 min.
7	Mare aged 750 lbs.	1 gr. Pilocarpine $\frac{1}{2}$ gr. Eserine 10 gr. $Ba.Cl_2$	Hypo-dermic	36 small	35 min. 30 strong	—	—	—	—	5-6-11-33-35 min.	—	—
8	Large Maltese Cat male	1-17 grain	Hypo-dermic	150	15 min. Impossible to count	102.4	15 min. 102 20 min. 101.8	60	15 min. 54 20 min. 120	None	2 min.	30 min.

Upon the pulse it is noted that it is at first quickened and then apparently shows a tendency to fall toward normal.

The normal temperature was reduced slightly in each instance. the range being from .2 to 1.3° and then gradually returning to normal.

In the majority the respirations were increased slightly. In a few of the cases some coughing was noticed after the injection of the drug.

The action of the drug upon the bowels was reasonably prompt and there seemed to be but little choice as to rapidity of action whether administered intravenously or hypodermically. The first effect was an increased peristalsis. In most of the cases there was flatus and where there was more than one evacuation of the bowels, the second was softer and more fluid than the first, indicating that tne intestinal glands were aetive.

In half of the cases urination took place, but attempts at micturition were frequent in all and seemed to be especially noticeable in the mares.

The pupils were contracted to mere slits and the lachrymal secretion was increased, in some instances running over the lower lid and through the nose.

The secretion of saliva was always increased, beginning in from 2 to 5 minutes and lasting from 45 minutes to one and a half hours.

Experiments Upon the Urine. The first experiments were tried upon human urine. The total amount of urine was collected each day for three days and an examination made each day. Then, for three days, five pills of pilocarpine nitrate, each containing 1-134 grain, were taken daily and the urine collected and examined as before. The average analysis of each of these three day analyses is herewith given.

	Before taking Pilocarpine (3 days)	While taking Pilocarpine (3 d.)
Amount	1850 cc.	1370 cc.
Sp. Gr.	1016	1022
Solids	37.28 grams—1000	51.26 grams—1000
Chlorides	3.85 " "	7.7 " "
Phosphates	1.96 " "	3.15 " "
Sulphates	4.00 " "	4.00 " "
Urea	15.00 " "	22.00 " "
Uric Acid	0.7 " "	0.48 " "

The same experiment was repeated later with the following results:

Amount	1363 cc.	1259 cc.
Sp. Gr.	1018	1024
Solids	41.94 grams—1000	55.92 grams—1000
Chlorides	9.4 " "	12.30 " "
Phosphates	1.96 " "	3.20 " "
Sulphates	4.00 " "	3.60 " "
Urea	11.00 " "	20.00 " "
Uric Acid	0.35 " "	0.30 " "

The tables show that there was an increased elimination of the solids during the pilocarpine period. The increase in the urea, chlorides and phosphates was especially noticeable. The sulphates varied little but the uric acid was somewhat decreased.

The same experiment was tried upon a large maltese cat. The solids were increased as before including in this instance quite a decided increase in the sulphates and a slight increase in the uric acid.

The urine of some of the horses was tested after the administration of pilocarpine and it was found that here also there was an increase of solids as compared with the average analysis of the normal urine.

An effort was made to determine how soon the urea increased in amount after the injection of the pilocarpine, the subject being a mare. Urine was drawn from the bladder at intervals and tested for urea. The following table shows the results:

Time	16 min.	1¼ hrs.	1½ hrs.	1¾ hrs.	2 hrs.
Amount of Urea	19 grams	34 grams	32 grams	28 grams	24 grams

A test upon another horse was carried out the same way:

Time	15 min.	1½ hrs.	¾ hr.	1 hr.	1¼ hrs.	1½ hrs.	2 hrs.
Amount of Urea	45 gms.	46 gms.	46 gms.	49 gms.	49½ gms.	49 gms.	46 gms.

It would appear that the maximum amount is reached in from 1 to 1 1-4 hours and then there follows a gradual decline.

In summarizing the effects of the drug upon the urine it would appear:

1. The amount of the urine is decreased, probably on account of the loss of fluid through other channels, (especially when sweating occurs).

2. The solids of the urine are relatively increased.

3. The urea excreted is increased in amount, reaching its maximum in 1 to 1 1-4 hours and then gradually decreasing.

4. The desire to urinate is increased after the administration of the alkaloid in both horse and man.

Saliva. The saliva of the horse does not show much digestive action upon starch under ordinary conditions. Some tests of this character were made to determine if the pilocarpine had any effect upon this action. While the results were somewhat variable, it appeared that, on the whole, the action was somewhat decreased.

Tests were also made to determine if any amount of urea was eliminated by the saliva. The results indicated that a slight amount was thus eliminated up to 20 minutes after the use of the drug and that there was then a decline. The proportion found did not exceed 2 grams per 1000 or 0.2%. So that the elimination of urea by this route would not appear to be of very great therapeutic importance. The secretion of the saliva was considerably increased in amount and usually began in from 4 to 7 minutes after the injection of the drug and continued from 3-4 to 1 1-2 hours.

CONCLUSIONS

There is an increase in the flow of saliva in the horse.

The amount of ptyalin in a given quantity of saliva appears to be decreased, perhaps on account of dilution.

The gastric and intestinal secretions are increased and the peristaltic movements are accelerated, and because of this combined action aid in overcoming impaction.

The blood pressure is lowered temporarily and the amplitude of the heart beat is increased.

The erythrocytes and leucocytes are both increased in number.

The respiratory movements are slightly increased and the bronchial secretion is augmented.

Body temperature is lowered.

The pupil of the eyes is contracted.

The amount of urine is diminished in quantity but the solids are increased, because of the loss of fluid through other channels.

MILK SECRETION AND DISEASES TRANSMITTED BY MILK

PIERRE A. FISH

The mammary glands are derived from the cutaneous glands. In a modified form they show some relationship to both the sweat and sebaceous glands. Toward the end of gestation, the secretory function of the mammae begins with the production of colostrum or the so-called "beast-milk." The colostrum is a thick, reddish or yellowish fluid with a more salty taste than that of normal milk and may serve as a purge to cleanse the alimentary tract of the newly born of the fecal material which has accumulated there previous to birth. This secretion contains numerous free fat globules and a large number of round shaped cells—the so-called colostrum bodies more or less filled with fat globules. Some cells are encountered that have a distinct amoeboid movement; these are leucocytes that have wandered through the epithelium into the glandular ducts and have taken up some globules of fat. In addition there are found some epithelial cells that have undergone more or less degeneration.

Colostrum differs from normal milk in its higher percentage of solids and especially in its higher percentage of globulin, albumin, nuclein compounds and lecithin. In a few days there is a decreased amount of globulin and albumin and the secretion of colostrum passes into the true milk secretion with a higher amount of casein so that at the expiration of about one week, the secretion possesses the characteristic appearance and composition of milk.

An old, but erroneous idea of the formation of milk was that it was simply an excretion—that its constituents were simply eliminated from the blood, like the urine. Another view was that it was composed of leucocytes which had wandered from the blood into the glands and there disintegrated and set free their contents. Still another view was that the epithelial cells of the gland itself were shed or sloughed off and gave up their contents to form the

milk. This view would necessitate the acceptance of the idea that the gland would have to regenerate itself once or twice during the twenty-four hours. This would mean an unusual activity and burden upon the tissues and is no longer tenable and it furthermore is not supported by satisfactory evidence. The modern view is that the mammary glands conform, in general, to the processes that have been worked out in the other glands of the body: that the material for the secretion is brought to the gland by the blood and that the cells elaborate this material and convert it into the constituents of the secretion. The fact that karyokinetic figures, evidencing cell division are occasionally seen indicates that cell destruction does occur to a certain extent and that these cells are reproduced, but this may occur in other glands as well.

The milk from animals of different species contains the same ingredients, *e.g.* water, proteids (especially casein and albumin), milk sugar (lactose), fat and inorganic salts. Quantitatively, there are marked differences between the milks of different species.

Casein is supposed to be the direct product of the gland tissue elaborated from the proteid of the blood by the action of the mammary cells, globulin from the serum globulin or the broken down portions of cells and the lactalbumin from the albumin of the blood. As to the lactose or milk sugar there are different opinions as to its formation. The view most commonly accepted is that it is formed in the gland from the sugar (dextrose) of the blood. Milk fat is derived partly from the fat in the food, partly from the fat tissues of the animal and from the mammary cells. These fats undergo a material transformation in the tissues of the gland, so that certain easily recognizable fats, even when taken up in quantity with the food, are either not visible at all in the milk or appear in very small quantity or are merely transitory. Doubtless milk fat—like fat tissue—may also be derived from the albumin or carbohydrates of the food. Citric acid, one of the minor constituents of milk does not originate in the food, but results from metabolism.

There is evidence that the mammary cells react to a number of different influences which may, within rather narrow limits, cause a changed composition of the secretion. On the whole milk is of a

rather definite chemical composition and this indicates that there is quite a definite adjustment between the cells of the gland and the secretion they produce.

The following limits of the constituents of cow's milk are very rarely exceeded: Water 83%—89%, Casein 2%—5%, Albumin 0.39%—0.95%, Fat 2.5%—7.5%, Lactose 4%—5.8%, Ash 0.35% —1.21%. Of these the fat shows a considerable range of variation and is commonly considered the most valuable constituent.

The term "total solids" includes all of the constituents of milk except the water. The total solids vary somewhat. During the summer months Dr. Van Slyke of Geneva, N. Y., found them lowest in May (12.56%) and gaining slightly each month until they reached their maximum in October (13.45%).

The difference in total solids of milk from some of the leading breeds has also been studied by Dr. Van Slyke, and his results are as follows:

Breed	Per cent. of water	Per cent. of Total solids
Holstein	88.20	11.80
Ayrshire	87.25	11.75
Shorthorn	85.70	14.30
Devon	85.50	14.50
Guernsey	85.10	14.90
Jersey	84.60	15.40

In milk from a mixed herd the water seldom falls below 86% and seldom exceeds 88%, although in a very few special cases variations ranging from a little less than 80% to a trifle over 90% are on record.

In the spring of the year, when cows are pasturing on new grass, or feeding on other succulent foods, they may yield milk containing a higher percentage of water as has already been shown by the research of Dr. Van Slyke.

Water distilled from milk is clear and colorless and has the same appearance as ordinary distilled water. The chemical reaction is the same (with Phenolphthalein). But there is considerable difference in the taste and smell. This indicates that some of the volatile substances of the milk are distilled over with the water.

Fat is usually considered the most important constituent of milk. It exists in the milk in suspension. According to numerous authorities, fat globules, at ordinary room temperature, are present in milk in liquid form. Cooling the milk to a low temperature (about 50 degrees F.) renders them firmer. The fat globules are very minute and vary considerably, according to breeds, individual cows, and the stage in the lactation period. The globules in the milk from the same cow also vary a great deal. According to Fleischmann, the size of fat globules varies between 1.6 micromillimeters and 10 micromillimeters. A Danish investigator finds from 2 1-2 to 11 1-2 million globules in a cubic centimeter of milk. Most authors find little or no difference in the kinds of fat of the different sized globules although some experiments seem to show that the fat of larger globules has a finer flavor, and a little more oily appearance.

Casein is the most important of the proteid constituents. It is the substance which forms the curd in cheese making. In fresh milk it is in chemical combination with lime salts. The viscosity of normal milk is believed to be due in a large measure to this condition of casein in milk. Casein differs from albumin in that the casein contains phosphorus and less sulphur.

When rennet is added to the milk of the cow, goat, buffalo and ewe the casein coagulates into a firm curd. When added to the milk of woman, mare and ass the casein precipitates as flakes. The former group includes animals with horns, the latter group is without horns.

Albumin or lactalbumin is very similar to the serum albumin of the blood, but differs in some particulars. It coagulates at about 158 degrees F. (70 degreesC.).

Lactalbumin occurs in milk in mere traces but in colostrum it is abundant. It coagulates at 167 degrees F. (75 degrees C.) and is very similar to the serum globulin of the blood.

Milk sugar or lactose is the most unstable constituent of milk. It quickly and easily decomposes by the action of micro-organisms. If these could be entirely excluded the milk would keep almost indefinitely. As it is difficult under practicable conditions to completely exclude the organisms from the milk, the only way in which

their growth can be retarded or prevented, and thereby prevent the changing of the sugar into other products, is to cool the milk to a low temperature (50 degrees F.) (10 degrees C.), or to heat the milk to a sufficiently high temperature (180 degrees F.) (82 degrees C.) to destroy most of the organisms. The sourness of milk is due to the decomposition of the milk sugar into lactic acid. A given quantity of milk sugar produces a somewhat smaller amount of lactic acid. This indicates that there are accompanying by-products during the decomposition of the sugar. Milk sugar is a white, and not very sweet powder. It is used largely in medicine in the preparation of pills and tablets.

The ash is obtained from the inorganic salts held in solution by the milk. Although small in amount they are important components. They consist chiefly of potash, lime, soda, magnesia and iron, combined with phosphoric, hydrochloric, sulphuric and carbonic acids. Calcium phosphate constitutes about one-half of all the ash constituents.

An enzyme, galactase, discovered by Babcock and Russel, exists in milk. This enzyme slowly peptonizes protein. Its significance and composition is not well understood. It has been suggested that it may come from the breaking down of the leucocytes.

Gases occur in the free state in milk. They consist of carbon dioxide, nitrogen and oxygen. The proportion and relation of the gases vary in freshly drawn milk and after it has been allowed to stand for a time. Certain gases are imparted to the milk by the gland and some are formed or absorbed in the milk later.

The gases formed by the gland are volatile and by cooling and aerating the milk they can to a large extent be eliminated. Certain taints of the milk may be due to the formation of gases, as when turnips, onions and garlic are fed to cows a short time before milking. The milk yielded by cows pasturing in the Alps is said to possess a peculiar, though not undesirable spicy odor and flavor. It is maintained by the Swiss that the peculiar flavor of the Emmanthaler cheese cannot be developed anywhere else in the world. This flavor they believe to be due to the kind of vegetation the cows feed upon in the Alpine pastures. Aside from the food, certain physiological disturbances may cause abnormal taints in the milk.

Gases or taints are absorbed into milk from its surroundings and great care should be exercised in keeping the utensils clean and the surroundings pure and wholesome. Gases may also be formed in drawn milk as the result of fermentation.

Variations in the quantity and composition of cow's milk may be due to numerous causes among which may be mentioned: breed peculiarities, individual peculiarities, the age of the cow, the stage of the lactation period, the time and method of milking, the influence of food, estrum, nymphomania, ovariotomy, abortion, exercise, disease and medicines.

Excretion of foreign material with the milk occurs to some extent but not so extensively as with some other glands, for example, the kidney. Mercury is easily excreted through the udder either when this substance is taken through the digestive organs or when absorbed after applications to the skin. Iodine and arsenic also easily enter the milk in considerable quantity. Opinions differ regarding alkaloids. It is a fact, however, that morphine, strychnine, atropine, and veratrine are, under certain circumstances, excreted with the milk in such large quantities as to be dangerous to the young. Other substances which can easily be excreted with milk are salicylic acid, carbolic acid, aloes, croton oil and senna, also the active principles of colchicum, hyoscyamus, and euphorbium. This is also supposed to be the case with mustard. Strong smelling medicines (asafetida ether and certain volatile oils) that are given to the cows may impart a taste to the milk.

It has been observed that diarrhea occurs in people who have used the milk of cows fed upon food that is moulded or that has undergone putrefactive fermentation. It is supposed that some of the substances which are formed under these conditions in the food materials of the cow may be excreted with the milk. Contamination of the milk and bacterial changes must, however, be always considered in this connection.

It is likely that toxic substances formed during disease, and such substances as may be reabsorbed from the uterus, may sometimes be excreted in the milk, but there is not much satisfactory information on this subject. On the other hand, we know that antitoxins are in part eliminated from the blood of the mother

animal through the udder and through this channel, they may be utilized by the young with benefit.

The keynote to all hygiene is cleanliness. Good food, pure air, clean surroundings and proper care are safeguards against disease. Under these conditions specific diseases are not easily introduced and general diseases are conspicuous by their absence.

There is probably no food product which should have more hygienic safeguards thrown around it than milk. The safety of the human race depends greatly upon it. Statistics have shown an appalling infant mortality when unfit milk has been used. Although pure milk is an ideal food for the young, it unfortunately appears to serve also as an ideal food for many of the organisms that prey upon the human race. The problem before the dairyman and the milk consumer at the present time is pure milk and all that it signifies.

Upon the veterinarian should fall the duty of adviser as to sanitary conditions. He should be fully cognizant of the infections that can be transmitted by milk to man; he should advise with the dairyman as to how they may be avoided. In this dual capacity he may serve as a protector of mankind and also guard the interests of the milk producer.

There are certain diseases common to cattle and man and there are certain organisms of disease common to man which may be introduced into milk and reinfect mankind.

Does milk, before it is drawn, contain bacteria that are pathogenic to man? When the disease affects the udder there is no hesitation in answering in the affirmative; but when the disease is without this local manifestation the question is not so easily answered. Some investigators maintain that such an elimination of bacteria occurs regularly, but others insist that this is not the case and that such an elimination is limited to cases where, during the course of the disease, there are local changes such as hemorrhage or inflammation appearing in the tissue of the udder. In foot-and-mouth disease the milk contains much infectious material; but the milk from cows with this disease shows a decided departure from normal, and it is not improbable that the elimination of infectious material may be associated with pathological changes in the udder.

In certain cattle diseases, pathogenic organisms may become mixed with the milk during milking, and from a practicable standpoint, this has the same significance as an excretion through the udder.

Some of the diseases of cattle which may cause a direct contamination of milk with pathogenic organisms is herewith appended:

Tuberculosis. Tuberculosis of the udder is of especial interest in connection with milk sanitation, because, when this condition is present, milk is always contaminated with tubercle bacilli. In uterine and intestinal tuberculosis a great number of bacilli are eliminated with the discharges and the excretions that soil the hindquarters, so these forms may easily cause infection of the milk indirectly. This also applies to some extent to animals that have tuberculous broncho-pneumonia.

Tubercle bacilli are sufficiently resistant to live through the souring and other processes necessary in the manufacture of milk into butter and cheese, so that these products may contain tubercle bacilli. This has been proven by a comparatively large number of butter tests.

The question as to the transmissibility of tuberculosis to man from milk and dairy products is of supreme importance. Koch, from his researches, has drawn the conclusion that the control of meat and milk, so far as tuberculosis is concerned is unnecessary. He considers that tuberculosis from food infection is rare in man. He doubts that tuberculosis can be transmitted from men to cattle. He is also doubtful that tuberculosis can be transmitted from cattle to man. Since the paper of Koch much research has been devoted to the points that he has brought to issue. This research has brought out the fact that tuberculosis by the food (primary tuberculosis of the intestines and mesenteric glands) is more frequent than he affirms, although statistics vary considerably. Furthermore, observations on animals, particularly on swine and monkeys, show that it is not wise to draw definite conclusions in relation to the mode of infection from the gross anatomical lesions. Thus, for example, with swine that are infected almost exclusively through the digestive canal, tuberculosis of the intestines is an exception, while miliary tuberculosis of the lungs often leads to a rapidly developing caseous pneumonia.

With regard to the production of tuberculosis in cattle from tuberculous material obtained from man, numerous investigations have shown that such transmission may be effected by inoculation.

The transmission of bovine tuberculosis to man seems to have been proven without much question. There are many observations, principally upon veterinarians and butchers, of tuberculous inoculation communicated to the hands and fingers through cuts while working with tuberculous organs of cattle. In some cases these were only local lesions that were healed by surgical means; in others the disease extended to the sheaths of the tendons and glands, and in still others, in the course of time, it appeared to develop into pulmonary tuberculosis. Greater interest is attached to cases of tuberculosis from food, which may with great probability be traced to infection through milk of tuberculous animals. A large number of such cases have been given, of which the following is one of the best proven instances: In a boarding school twelve young girls became ill with signs of intestinal tuberculosis and five of them died. All came from healthy families and no source of infection was found but one cow which supplied milk for the school and was shown to be affected with tuberculosis of the udder.

If one considers that tuberculosis from food is not infrequent in man, and occurs quite frequently in children, that human tuberculosis is often transmissible to cattle, and that clinical knowledge argues for transmission of bovine tuberculosis to man, and if one considers that tubercle bacilli from cattle have been proven at least as dangerous and generally more virulent for all animals than tubercle bacilli from man, then milk containing tubercle bacilli must be regarded as most dangerous to health and the utmost care should be taken to prevent the sale of such milk.

Foot-and-Mouth Disease. It has long been known that milk from cows suffering with this disease is infectious and may carry the disease to man. In the lighter forms of the disease the milk remains unchanged, but with cows badly affected there is not only a decided diminution in quantity but its appearance and composition are changed. In such cases the milk becomes thin, separates a slimy layer of cream of dirty color, and there is quite abundant sediment, or, as happens infrequently, it becomes richer in fat with

a simultaneous falling off in quantity. Under the microscope, leucocytes and broken down tissue cells are found in greater quantity than usual, sometimes red corpuscles also. The milk contains a greater quantity of albumin and globulin than usual, so that when boiled, large clumps and flakes separate and the sugar and casein fall off in quantity—all changes which are symptomatic of an admixture of an inflammatory exudate. The virus may, moreover, enter the milk as it is being drawn, if vesicles occur on the teats or udder. The quantity of milk decreases notably during the course of the disease and it seldom reaches its original flow after recovery.

This disease is very easily communicated by the milk to other cattle and to swine as well as man. Children are especially susceptible. The course of the disease in man may be light or severe and may cause death. The symptoms are: fever and weakness, conjunctivitis, formation of vesicles on the mucous membrane of the mouth, the lips, the ears, the nose, fingers or, less frequently, on other places on the body; besides nausea, vomiting, diarrhea; sometimes redness of the skin and arthralgia. It is transmissible from man to man. The virus of foot-and-mouth disease may occur in butter, buttermilk and cheese, since it is not killed by the treatment which milk undergoes in their production.

This virus, the appearance of which is wholly unknown (probably on account of its ultramiscroscopic size), is not particularly resistant. It has been proven by experiments made during recent years in Germany that the virus dies after 10 minutes' exposure at 158 degrees F. (70 degrees C.) and by being heated at 212 degrees F. (100 degrees C.) for an instant.

Cowpox. This disease attacks the teats of the cow particularly and it cannot be doubted that during the milking the virus held in the vesicles sometimes falls in the milk. Since the vaccine virus is known to be very potent, and since man is peculiarly susceptible to it, it is evident that the disease is transmissible through milk to man. But, while there are numerous examples of direct infection on the hands and face of the milker, there are only a few observations of an infection through the use of such milk. This is probably due to the fact that most persons are early immunized by compulsory vaccination and that small children usually drink the milk

after it has been boiled or, at least, heated. Stern reports a case in which a large number of children became affected with an eruption on the face, which healed, leaving scars, after using milk from a herd of cows in which cowpox had broken out.

Anthrax. During the course of anthrax, the secretion of milk falls off suddenly and decidedly. The milk secreted is thin and its composition is supposed to be abnormal. Several investigators have observed that the milk of cows affeeted with anthrax contains virulent bacilli. Others have found that this is not always the case. Because the milk is often mixed with blood, following slight hemorrhages in the udder, it is probable that the admixture of bacilli occurs chiefly when such hemorrhages take place. Raw milk should not be used from a herd in which the disease has broken out as there is danger that the bacilli may enter the milk when it is drawn, because the sick animals exerete bacilli with the bloody excrement and the stable, in spite of all care and disinfection, may be so thoroughly infected that there is the possibility of contaminating the milk.

Rabies. The virus of rabies, yet unknown, is especially associated with the central nervous system and the salivary glands. Frequently it may be found in other glands and even in the udder. A number of observers have proven that the virus may be secreted with the milk. All attempts to convey the disease to healthy animals, through food containing infectious material have thus far been negative, and many hold the view that there is no danger to man from the use of milk from cows that have been bitten by a mad dog and that are themselves rabid.

Since the possibility is always present that infection may occur through a slight lesion of the mouth or pharynx, milk from cows infected with rabies is to be regarded as most dangerous to health.

Actinomycosis. There are no recorded observations concerning the changes in milk secretion during this disease, nor have the actinomyses or ray fungi yet been found in milk, in which they probably occur. Man may be infected through the digestive canal just as cattle are, and on this account the possibility of contagion through milk should not be disregarded. Milk from cows affected with udder actinomycosis (which is not often diagnosed) should not be used as food for man.

Other diseases which may infect the milk sufficiently to make it unsafe for food are: lung plague, mastitis, "calf cholera" septic metritis, suppurative processes, milk sickness (Central U. S. Formerly confused with anthrax).

Milk may furthermore be contaminated with organisms of diseases specific to man. Serious and extensive epidemics have arisen in this way. Contamination may take place during milking, during its handling on the farm, or later, while it is being handled or stored in the dairy or market place. Sometimes this occurs from sick persons coming directly in contact with the milk, sometimes it occurs in an indirect way. The method of contamination differs in respect to different diseases, since infectious material may come not only directly or indirectly from persons but may also come from the water used for cleansing the milk vessels.

The human diseases which may thus be indirectly communicated ta mankind through milk are: typhoid fever, diphtheria, scarlet fever, Asiatic cholera, tuberculosis and there are even reported instances of the transmission of syphilis, and epidemics of sore throat and of erysipelas through milk. The transmission of measles, smallpox, dysentery, or cerebro-spinal meningitis has not been observed, but the possibility of such transmission can scarcely be doubted.

The possibility of so many infections coming directly and indirectly from milk illustrates the great importance of dairy hygiene. This importance is becoming more and more appreciated and the day is not far distant when the services of cultured and competent men will be increasingly in demand to protect the interests of the dairymen and to safeguard the public health. These men should be veterinarians.

PHYTOLACCA DECANDRA

ROGER D. HYDE

According to the locality in which it grows and the uses to which it is put Phytolacca has numerous synonyms. The following are those most frequently encountered: Poke, poke berry and root, garget, garget berry, cocum, coacum, jalap, skoke, scote, scoke jalap, American nightshade, red nightshade, cancer root, jalap cancer root, chougras, red weed, red ink plant, red ink berry, crimson berry plant, pocan bush, Virginia poke, mechoacan, American currant, dyer's grapes. In Germany it is known as the scharlachbeere and kermesbeere. In France it is known as agouman, morelle a grappe. In Spain it is called namoli, jabonera.

The word Phytolacca is derived from the Greek word "phyton"—a plant—and the Latin word "lacca"—lake—having reference to the crimson color of the juice of the berries.

Phytolacca is native to the United States, from Maine and northern Illinois to Florida and west to Texas, eastern Kansas and southern Minnesota. It is also found in northern Africa, China, southern Europe, the Azores and Sandwich Islands. In America it grows commonly along fences bordering fields, in rich, moist uncultivated spots or waste grounds; also in clearings along roadsides. It has been regarded as a weed in the United States, but in Europe it is valued as an ornamental garden plant.

The plant is a smooth, rank, succulent perennial and reaches a height of six to eight feet, although in the Southern States it may grow as high as twelve feet. The root is very long, woody and thick, like the horseradish root. The stems of the plant are purplish green and hollow, with thin transverse partitions at intervals. The leaves are large and alternate. There are numerous clusters of small greenish white flowers, which blossom throughout the summer, and are followed in the autumn by shining purple black berries. From the root is obtained a rich purple juice, which, in Europe, is sometimes used to color wines. The root contains numerous starch

grains, tannic acid, gum, sugar, resin, a fixed oil, lignin and various inorganic substances. The root should be gathered in the latter part of the autumn, washed, sliced and carefully dried. It loses strength with age.

The leaves make the plant, with its height and purple berries, a very beautiful and striking plant. They should be gathered just before the fruit ripens. The leaves are said to have the property of destroying epitheliomata. For this purpose they are bruised to a pulpy mass and the juice from them is collected on a plate, evaporated to a thick, pasty consistency. It is then spread upon a cloth and laid upon the tumor. It is supposed to have a selective action upon the morbid tissue and to cause its liquefaction and removal. It then acts as a cicatrizant for the open sore. As soon as all morbid tissue is destroyed a bed of cicatricial tissue begins to form from the periphery towards the center and, as this occurs, the plaster should be cut smaller each day, like the shape of the healing tumor. It is claimed that a large tumor can be cured in a few weeks in this manner.

The fruit or berries form close and heavy agglutinated purple black masses. There is little odor but there is an acidulous, sweetish, acrid taste. Some claim that the berries are poisonous, others that they are harmless, but that the seeds are harmful. Birds are known to eat the berries without injury. The berries are said to lose their toxic power somewhat when cooked and some people have made pies of them, but this practice is not to be recommended. Nearly all claim that the juice of the berries is harmless and the Turks are said to have used it for tinting candies. The juice contains sugar, which when fermented yields alcohol by distillation.

The chemical composition of phytolacca is peculiar. Its active and poisonous constituent is a bitter acrid substance, similar to, if not identical with, saponin. The root is remarkable for the great amount of potassium in it. It exists as potassium oxide and nitrate to the amount of 5.56% in the dried root. A splinter gives a violet coloration in the Bunsen flame.

A quantitative analysis of poke root is given as follows: fatty oil and wax 0.6%; bitter resin 1%; non-reducing sugar 0.4%; proteids 1.94%; amido compounds 1.6%; probably free formic acid

0.36%; potassium formate 1.9%; starch 11.68%; calcium oxalate 6.2%; nitrates 2.4%; cellulose 16.4%; lignin 3.2%; gum, coloring matter, ash and moisture 42.75%.

Claussen obtained from the seeds a neutral principle, which he called phytolaccin.

The parts of the plant used officially are the fruit and the root. The leaves are sometimes used in the form of decoctions and poultices, and the juice in plasters. There are resinoid preparations of the berries which are said to be the basis of the so-called anti-fat cures.

Antagonists to phytolaccin are alcohol, ether, opium, digitalis, strychnine and atropine.

The synergists are the motor depressants, emetics and paralyzers. Externally the powdered root is irritating to the mucous membrane of the nose causing sneezing and burning, and may produce in certain subjects erythematous eruptions and excoriations.

Digestive System. Phytolacca is an emetic and cathartic. It causes great nausea, with much depression, lasting some time before vomiting occurs. Besides being a laxative it augments the secretion of the bile. Brunton claims that it is a powerful hepatic stimulant.

Upon the circulatory system, it reduces the force and frequency of the heart's action and lowers arterial tension.

Upon the nervous system, phytolacca is a powerful motor depressant. It acts as a direct paralyzant to the spinal cord and medulla. It is said to be somewhat hypnotic.

The respiration is depressed and the breathing becomes slow and shallow. Toxic doses cause death by paralysis of the respiratory center.

The drug is readily absorbed by the digestive organs and eliminated principally by the kidneys.

Poisoning. Most instances of poisoning arise when the plant has been used as a medicine by laymen, but there are also accidental cases due to eating the root which has been mistaken for artichoke, parsnips or horseradish. Some claim that the plant is one of our most violently poisonous plants, especially when fresh. In early

spring before the foliage comes, the roots are sometimes grated and eaten, being mistaken for horseradish and toxic results follow. The greens are also sometimes eaten and thorough cooking seems to destroy their toxic effects, but if incompletely cooked poisoning will occur.

The symptoms of poisoning are vertigo, swelling of the eyelids, watering of the eyes, photophobia and dimsightedness. There may be the sensation of roaring in the ears. Pain in the muscles and bones of the arms. There is weakness of the heart, intermittent pulse and occasional pain in the cardiac region. There may be coryza, a sensation of constriction in the larynx, coughing and difficult breathing.

There may be either diminished appetite or unusual hunger, violent thirst, eructations, nausea and repeated and violent vomiting, (human), pain in the stomach and violent pain in the regions of the liver and kidney, colic, frequent discharges of offensive flatus, infrequent diarrhœic stools which may be painless or with tenesmus.

There is increased urination with the color considerably darkened and with increased deposits.

In the Journal of Comparative Medicine and Veterinary Archives for July, 1902, Dr. G. R. White describes a case of poisoning in cattle by phytolacca. He found that the cattle had not eaten for four days. They were at first constipated but later passed mucus and clots of blood from the bowel. The animals were spiritless and held their noses close to the ground. Their eyes were sunken, backs arched, high fever and their muzzles were dry and hot and there was also a slight discharge from the nose. There was loss of appetite, cessation of rumination and a staggering and weak gait. The disease was at first pronounced hemorrhagic enteritis with dysentery, but upon investigation the field where the cattle had run two days, thousands of poke plants were found, hundreds of which had been eaten off even with the ground. The evidence seemed fairly conclusive that the plants were the cause of the trouble.

The Treatment is to give absolute repose and warmth, as movements are likely to induce retching. The stomach should be emptied by means of a stomach pump and morphine administered hypodermically to lessen the pain of the cramps and to support the heart.

Strychnine may be given to stimulate the respiration. Antiemetics are also indicated.

Therapeutics. Phytolacca is credited with being one of the best remedies for the treatment of mammitis. It may be given both internally and externally for this purpose. It has also been recommended for ring worm, ulcers, scabies and favus. Brunton recommends its use in the form of a strong decoction or infusion of the root for piles, skin diseases and cancer. It has also been used to allay inflammation, as in follicular pharyngitis, tonsilitis, buboes, burns, abscesses and chronic edema. Its use internally and locally has been recommended for sore nipples, orchitis, varicose ulcers, parasiticide and as a dressing for cancers.

It is claimed that birds which ate phytolacca berries were seen to lose flesh. The drug is said to act upon the lacteal vessels and mesenteric glands so as to retard the taking up of the fatty elements of the food by the lacteals and an insufficient elaboration of their contents by the mesenteric glands, so that this important channel of nutrition is less active. In this way the drug is said to act as an antifat.

The drug is *contraindicated* in subacute or chronic conditions, or when the heart's action is weak, or when there are catarrhal conditions in the stomach. The contraindications are much the same as for aconite or veratrum viride.

Experimental. In order to test the antifat action a fat tom-cat was experimented upon. This cat had been castrated three or four years previously when a kitten, and in the meantime had become quite obese. The experiment covered a period of eight weeks and the cat was weighed daily and the average taken for each week. On the second, fourth, sixth and eighth week the cat received increasing doses of the fluid extract of phytolacca. The range of the dosage was from five minims the first week to twenty minims, twice daily, during the last week. During the odd weeks there was no medicine whatever administered.

The average weight for the first week was 9 lbs. 2 ozs. For the next week, while the medicine was administered, the average weight increased 1 lb. 9 ozs. The average for the third week showed a de-

crease of 11 ozs.; for the fourth week (phytolacca) a decrease of 10 ozs.; for the fifth week a gain of 11 ozs.; for the sixth week (phytolacca) a gain of 7 ozs.; for the seventh week a gain of 2 ozs.; for the eighth week (phytolacca) a gain of 2 ozs. At the end of the experiment the cat weighed on the average 1 lb. and 10 ozs. more than he did before the drug was administered. The result was unexpected. Some other preparation than the fluid extract might have been more efficient for fat reduction and the fact that the animal had been castrated may also have had some bearing on the result.

Another experiment was tried upon a normal kitten which weighed 2 lbs. and 1-2 oz. The kitten was given 10 minims of the fluid extract of phytolacca and on being weighed two days later was found to have lost 2 ozs. Increasing doses were given up to 1 dram and at the end of the experiment the weight of the animal was found to be 1 lb. 12 ozs., a loss of 4 1-2 ozs. The larger doses caused restlessness, depression and purging but with eventual recovery.

Ten experiments were tried upon horses in order to determine the effect of phytolacca upon the temperature, respiration and pulse. The following details of experiment No. 6 appear to be typical of the most of the experiments and are herewith given. The animal was a light bay gelding weighing about 1000 lbs. One ounce of the fluid extract of phytolacca was administered in a half pint of water at 9 a. m.

		Temperature	Respirations	Pulse
(Normal)	9:00 a. m.	100.4	14	47
	9:30 a. m.	100.4	13	46
	10:00 a. m.	100.8	14	33
	10:30 a. m.	100.9	15	32
	11:00 a. m.	100.6	15	37
	11:30 a. m.	100.1	15	44

The animal passed wind but suffered no distress. There was no diarrhea and the following day the feces were of normal consistency.

The dosage ranged from 1-2 to 2 1-2 ozs. of the fluid extract. In only one case was there diarrhea and this persisted for two days. Two other horses showed evidences of slight diarrhea but it was not at all persistent. In nearly all cases there appeared to be increased peristalsis and more or less flatus.

The effects upon the temperature, respiration and pulse were not uniform. In some cases there was a slight increase and in others a decrease, but the variations in all were confined to narrow limits.

Experiments upon the heart of the frog showed that the drug had a depressing action and finally caused paralysis of that organ.

An experiment was tried upon a human subject in order to determine the effect upon body metabolism as shown by variations in the urinary excretion. The experiment covered a period of five weeks, the urine being examined each day for six days of each week. The examinations for the first week were upon the normal urine. In the second week the drug was begun in doses of 10 drops of the fluid extract after each meal. The dosage was increased until in the latter part of the fourth week 50 drops were being taken. None of the drug was taken during the fifth week, but the urinary examinations were continued in order that a comparison might be made between the fore-period (normal), drug period and after-period. During the third week while 35 drops were being taken a slight sensation of dizziness was experienced each time the drug was taken. The medicine was, however, continued in increasing doses but there were no further effects of this character. Throughout the entire experiment the drug did not produce an emetic or purging effect, but it seemed to increase the appetite.

	Average for Fore Period	Average for Drug Period	Average for After Period
Amount for 24 hours	666 cc.......	740 cc.......	616 cc.
Specific gravity.............	1025	1025.5	1028.6
Reaction.....................	Acid	Acid	Acid
Solids (24 hours)...........	38.62	43.47	66.8
Chlorides (24 hours)........	10.32	13.58	18.74
Phosphates (24 hours).......	1.75	1.80	3.32
Sulphates (24 hours).......	1.89	2.08	2.28
Urea (24 hours)............	17.75	18.37	16.6
Uric Acid (24 hours)........	.27	.43	.42

There was a trace of indican, a few pavement epithelial cells and crystals of calcium oxalate found throughout the whole experiment.

In addition to the uses of the drug already enumerated it was

used in the form of an ointment upon some dogs suffering from skin trouble. The ointment was made up in the proportion of 1 oz. of the powdered root to 7 ozs. of benzoinated lard. This was found to be somewhat irritating and the proportions were reduced to 1 to 12. The effect was beneficial in some cases but not in all.

The drug is of undoubted value especially as an alterative and is of considerable use in those cases in which it is especially indicated.

TABLE OF CONTENTS.

CANINE TETANUS.

Pierre A. Fish.

A St. Bernard dog aged nine months was brought to the clinic. The owner stated that the dog had some difficulty in swallowing and as the throat appeared slightly swollen he suspected that the trouble might be sore throat. A calomel purge was given without effect. No evacuation of the bowels occurred until the fourth day. In the meantime, injections of 1/10 grain eserine and 1/6 grain pilocarpine had been administered, accompanied by epsom salt enemas.

When entered, the symptoms of tetanus were not very positive; but very shortly the stiffness of the body increased quite perceptibly, the membrana nictitans covered a portion of the eyeballs and the ears were somewhat retracted and drawn toward the median line, causing the skin of the forehead to wrinkle. The nose was somewhat uplifted as if the animal were sniffing. This retracted condition was probably due to the stiffening of the nasal muscles.

The dog's condition appeared to remain stationary for a few days. Shortly before the patient was received, the writer had read with much interest an article by Dr. Wilber Fisk Sterman on "The Surgical Treatment of Tetanus." References were made in this article to the cure of some horses by this procedure. The theory of the treatment appeared to be that in addition to, or independently of, any formation of toxin, the cause of the trouble was gas, developed by the organisms, and that the gas was found to be present in unusual quantity beneath the meninges of the brain or, as a later reference intimated, even in the ventricles of the brain. Under these conditions, when the cranium was trephined and the dura penetrated, there would be quite an audible hiss from the escaping gas. In some cases this was said to result in quite rapid recovery without further treatment. In other cases it might be necessary to penetrate through the nervous tissue or as one reference put it, to "bore for gas," as far as the ventricle.

The case in hand seemed to offer an excellent opportunity for testing the surgical treatment of the disease. The dog was placed under the influence of anesthetics and with a trephine a small button of bone was removed from the cranium just to the right of the

longitudinal fissure between the two hemicerebrums. The dura was opened but there was no evidence of escaping gas. The surface of the brain was touched and a small portion of the pia loosened but with no trace of gas. The surface of the brain, however, seemed unduly irritable whenever touched. The opening in the cranium was left. The skin was not sutured until a half hour later and then with only a stitch or two, in order that if any gas should perchance be escaping there might still be an exit for it. It was thought that healing might be delayed until all of the gas had escaped.

Shortly after the operation the writer was called out of town for a short time. Directions were left for the care of the patient. Two days after the operation the dog was chloroformed to death in order to relieve his suffering. The writer was informed that the dog did not improve after the operation but grew steadily worse until chloroformed.

During the course of the treatment a sore was found upon one of the dog's toes, where, probably, the infection began. The wound received the usual carbolic acid treatment.

FIG. 1. *A photograph of the patient. The stiffened attitude, the half closed eyes, the upraised nose and the drawing of the ears toward the median line are more or less clearly shown.*

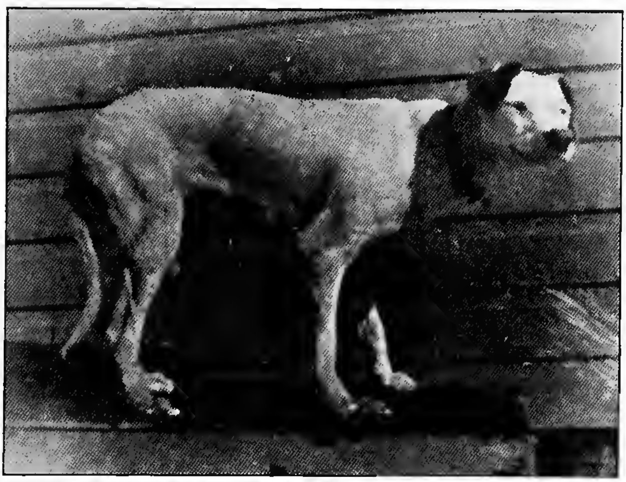


FIG. 2. *Another case of tetanus in the dog. The symptoms and conditions are similar to those in figure 1. The nose is somewhat more retracted. The muscles are tense and because of the short hair the outline of certain muscles or groups of muscles are quite distinctly visible through the skin, especially in the hind quarters.*

THE DIASTASES IN THE SALIVA OF THE DOG AND CAT.

CHARLES E. HAYDEN.

Literature.—There is a large amount of literature pertaining to the salivary glands, their secretions and the active principles of these secretions. Conditions which influence secretion have also been given a great deal of attention.

Early day investigators dealt with many of the same questions in regard to salivation which are holding the attention of present day workers. Bernard was one of the earliest and foremost to engage in this problem.

One paper of indirect interest in connection with this work is that of Carlson, Greer and Becht [1] showing the relation of the blood supply to the submaxillary glands and the character of the chorda and sympathetic saliva. Heidenhain's theory of the trophic nerves is here disputed and held to be untenable. They find that decreasing the blood supply decreases the quantity of saliva and increases the solid constituents of both chorda and sympathetic saliva.

Another paper of like interest is that of McLean [2] giving evidence of vaso dilator fibers to the submaxillary gland of the cat.

Still another bearing on the same subject as the preceding is the joint work of Carlson and McLean.[3] They present further evidence of the relation of oxygen supply to the salivary glands to the composition of the saliva. Their evidence shows that decreasing the oxygen supply increases the solid material in chorda and submaxillary saliva.

In dealing with the blood supply these papers are pertinent to the subject matter in that they show some of the manifold conditions affecting the rate, quality and quantity of the salivary secretions.

The diastases in the blood and lymph are shown to vary in concentration in the following order in the various fluids named: serum, thoracic lymph, neck lymph, leg lymph, pericardial fluid and cerebrospinal fluid.

As a supposition the liver is said to be the possible organ of

the production of the diastases. The portal and hepatic veins, however, are said to have the same amount of diastatic ferment. Extirpating the pancreas eliminates it as an organ of production, for it does not lessen the amount of diastase in the blood fluids. They are increased under anaesthesia due to possible increased destruction and elimination and decreased production.

As a result of elimination the urine often shows a diastatic effect. Numerous experiments made by the authors upon cats, dogs and chickens fed upon a carbohydrate diet show that there is no relation between the concentration of the enzyme and the natural diet. The enzymes of the blood and lymph are stated to be the discards of the tissues in general and of no particular organ of the body.

Following the preceding statement that there is no relation between the concentration of the enzymes and natural diet, it is well to consider the results obtained by four different pairs [5] of experimenters upon the adaptation of the salivary secretion to diet. Of these, three pairs [6] find results that show adaptation, one pair [7] finds results that do not. Two [8] deal with the human saliva, two [9] with that of the dog and cat. The last two find results that are of interest in connection with the subject matter of this paper. One pair [10] maintains that the dog's saliva is inactive under carbohydrate diet, the other [11] that the saliva is active under the same conditions, and in eight different animals tested, they report sugar ranging from .0133 to .054 gram.

Reducing substances [12] have been demonstrated in the submaxillary and parotid saliva of the cat and the substance is shown to be glucose by crystal formation and by the fact that these crystals melt at a temperature very near that of the melting point of glucose. The glucose of the saliva is said to be that of the blood eliminated by the salivary glands. The claim is made that the submaxillary secretes more sugar than the parotid gland and that the amount is increased under ether anaesthesia. The last fact is accounted for by the production of a condition of hyperglycemia.

Work has been carried on by A. J. Carlson and J. C. Ryan [13] upon the saliva of the dog and cat. They demonstrated the presence of an enzyme in the saliva of the cat. They say that in all proba-

bility there is none in that of the dog. Most of the work was carried on with the saliva of the cat. Only a few experiments with that of the dog. The concentration is found to be greater in reflex or chorda or pilocarpine stimulation under ether anaesthesia than in any other condition. Concentration is greater in almost every instance in the sympathetic than in the chorda saliva. The same condition prevails comparing the blood serum with the saliva. Human ptyalin and pancreatin injected into the blood increased the enzyme, giving rise to the hypothesis that blood and lymph furnish the enzymes of the salivary gland. Only two of their experiments show a starch splitting ferment in the saliva of the dog.

Method.—Seven sets of tests were made in this investigation. Salivary extract was tested qualitatively and quantitatively for the presence of sugar. The quantity of reducing sugar in the salivary extract with and without starch digestion; in the serum under the same condition and the quantity resulting from the digestion of starch with saliva have been made the basis for the conclusions drawn in our experiments. The method of obtaining the salivary extract was the same throughout. The glands were macerated in 1% acetic acid, one cc. for each gram of gland substance and then ten cc. of chloroform water was added for each gram of gland substance. The maceration was carried on as carefully as possible and the extract allowed to stand at least twenty-four hours before testing. The saliva was obtained in several different ways. Pilocarpine was used on two cats and an attempt made to use arecoline upon another. These two drugs were found unsatisfactory. The animals struggled too much, and since cannulae were not inserted in the salivary ducts they swallowed most of the saliva making it difficult to collect. Both drugs made the cats sick after a short time. The method finally adopted was that of light ether anaesthesia.

A few cc. of the saliva were collected. The saliva was always tested at once with 1% starch solution and was incubated for a period of 120 minutes or longer at a temperature of 37 or 38° C. There were some variations in time and slight ones in temperature in a few of the experiments. The serum was not taken from the animals on the same day as the saliva but it was obtained as clear as possible. The blood in some experiments was taken from that

passing through the heart and in others from the carotid artery. As a reagent for reducing sugar we first used Fehlings. It was difficult, however, to standardize for quantitative work and proved less satisfactory than Benedict's [14] solution which was the one used. It is composed of three solutions.

Solution A.	Crystalized $CuSo_4$................	69.3	gm.
	Distilled water to................	1000	cc.
Solution B.	Crystallized Rochelle salt........	346	gm.
	Pure anhydrous Na_2Co_3..........	200	gm.
	Distilled water to...............	1000	cc.
Solution C.	Potassium sulphocyanide.........	200	gm.
	Distilled water to................	1000	cc.

The formula for a fourth solution is given by the author. The solution is to alternate with solution C. and its purpose is to make the test more sensitive when foreign substances such as chloroform are found in the fluid to be tested for sugar.

Solution D.	Potassium ferrocyanide............	30	gm.
	Potassium sulphocyanide..........	125	gm.
	Anhydrous Na_2Co_3.................	100	gm.
	Distilled water to.................	1000	cc.

A solution containing sodium carbonate is said to have the advantage over one containing sodium hydrate in that it does not decompose so readily. The third solution gives a white precipitate when all the copper in the solution has been reduced. The three solutions are mixed in equal proportions and are more sensitive than Fehling's solution. From two to five grams Na_2Co_3 are an aid in testing for dilute sugars. Two sets of solutions were used, the first being standardized to .076 gm. sugar for each 10 cc. of copper solution. The second to .078 gm. Our practice when testing for sugar was to add a certain number of cc. of the solution under digestion and then add enough 1% dextrose from a burette to completely reduce the copper solution.

The method of computing the number of grams of reducing sugar per cc. in the digested solution was as follows:—Suppose 6.6 cc. of 1% dextrose were added to the reagent mixed in the proper proportions, after adding 10 cc. of the digested product.

6.6 cc. of 1% sugar equaled .066 gm. of sugar. .076 gm. minus .066 gm. equals .01 gm. sugar in 10 cc. of the solution and so would show .001 gram to each cc. of serum, saliva and salivary extract used.

TABLE I.

Animal	Material used	Amt. 1% starch used	Time of digestion	Test for sugar	Results
Dog 1.	Salivary extract	25 cc.	90 min.	Fehling's	+
Dog 2	Salivary extract	25 cc.	90 min.	Fehling's	+
Dog 3	Salivary extract	25 cc.	90 min.	Fehling's	+
Dog 4	Salivary extract	25 cc.	90 min.	Fehling's	+
Polecat 1	Salivary extract	25 cc.	90 min.	Fehling's	+
Polecat 2	Salivary extract	25 cc.	90 min.	Fehling's	+

TABLE II.

Animal	Material tested	Amount 1 per ct. starch used	Amount salivary extract used	Time of digestion	Amount 1 per ct. dextrose used	Reagent used	Amount sugar per cc. extract
Dog 1	Salivary ext.	25 cc.	25 cc.	120 m.	4 cc.	Benedict's	.00144 gm.
Dog 2	"	25 cc.	25 cc.	120 m.	5.6 cc.	Benedict's	.0008 gm.
Dog 3	"	25 cc.	25 cc.	120 m.	6.6 cc.	Benedict's	.0004 gm.
Dog 4	"	25 cc.	25 cc.	120 m.	6 cc.	Benedict's	.00064 gm.
Dog 5	"	25 cc.	25 cc.	120 m.	6.4 cc.	Benedict's	.00048 gm.
Cat 1	"	25 cc.	25 cc.	120 m.	2 cc.	Benedict's	.00204 gm.
Cat 2	"	25 cc.	12.5 cc.	120 m.	4.6 cc.	Benedict's	.0024 gm.

TABLE III.

Animal	Substance tested	Amt. serum used	Amt. 1% dextrose usedcc.	Amt. sugar per cc. serum
Dog 6	Serum	5 cc.	6.4 cc.	.0028 gm.
Dog 7	Serum	5 cc.	5.4 cc.	.0048 gm.
Dog 8	Serum	5 cc.	6.6 cc.	.0024 gm.
Cat 3	Serum	2.5 cc.	6.6 cc.	.0048 gm.
Cat 4	Serum	10 cc.	5.6 cc.	.0022 gm.
Cat 5	Serum	1 cc.	7.8 cc.	None
Cat 7	Serum	1 cc.	7.8 cc.	None
Cat 8	Serum	3 cc.	6.6 cc.	.004 gm.
Cat 9	Serum	6 cc.	6 cc.	.003 gm.
Cat 10	Serum	2 cc.	6.6 cc.	.006 gm.
Cat 11	Serum	3 cc.	6 cc.	.006 gm.

TABLE IV.

Animal	Substance tested	Amt. 1 per ct. starch used	Amt. serum used	Amt. 1 per ct. dextrose used	Reagent used	Amt. sugar per cc. serum
Dog 6	Serum	25 cc.	5 cc.	1 cc.	Benedict's	.0133 gm.
Dog 7	Serum	25 cc.	5 cc.	1 cc.	Benedict's	.0133 gm.
Dog 8	Serum	25 cc.	5 cc.	None	Benedict's	.078 gm.
Cat 3	Serum	60 cc.	2.5 cc.	5.6 cc.	Benedict's	.0088 gm.
Cat 4	Serum	60 cc.	10 cc.	None	Benedict's	.078 gm.
Cat 5	Serum	25 cc.	1 cc.	4 cc.	Benedict's	.038 gm.
Cat 7	Serum	25 cc.	1 cc.	4.2 cc.	Benedict's	.036 gm.
Cat 8	Sernm	25 cc.	3 cc.	3 cc.	Benedict's	.016 gm.
Cat 9	Serum	25 cc.	6 cc.	None	Benedict's	.013 gm.
Cat 10	Serum	25 cc.	2 cc.	2 cc.	Benedict's	.029 gm.
Cat 11	Serum	25 cc.	3 cc.	2 cc.	Benedict's	.013 gm.

Time of digestion 120 min.

TABLE V.

Animal	Substance tested	Amt. 1 per cent starch used	Amount saliva used	Time of digestion	Amt. 1 per ct. dextrose used	Reagent used	Amt. sugar per 1 cc. saliva
Dog 6	Saliva	25 cc.	5 cc.	120 min.	7.8 cc.	Benedict's	None
Dog 7	Saliva	25 cc.	2 cc.	120 min.	7.8 cc.	Benedict's	None
Dog 8	Saliva	25 cc.	5 cc.	120 min.	7.8 cc.	Benedict's	None
Dog 9	Saliva	25 cc.	10 cc.	17.5 hrs.	5.8 cc.	Benedict's	.002 gm.
Cat 4	Saliva	25 cc.	3 cc.	120 min.	6.6 cc.	Benedict's	.004 gm.
Cat 5	Saliva	25 cc.	1 cc.	120 min.	6.8 cc.	Benedict's	.01 gm.
Cat 6	Saliva	25 cc.	2 cc.	120 min.	7 cc.	Benedict's	.004 gm.
Cat 7	Saliva	25 cc.	2 cc.	120 min.	6.8 cc.	Benedict's	.005 gm.
Cat 8	Saliva	25 cc.	3 cc.	120 min.	5.8 cc.	Benedict's	.0066 gm.
Cat 9	Saliva	25 cc.	6 cc.	15 hrs.	6.4 cc.	Benedict's	.0023 gm.
Cat 10	Saliva	25 cc.	2 cc.	120 min.	6 cc.	Benedict's	.009 gm.
Cat 11	Saliva	25 cc.	3 cc.	120 min.	6.8 cc.	Benedict's	.0033 gm.

TABLE VI.

Animal	Substance tested	Amt. extract used	Reagent used	Amt. 1 % dextrose used	Amt. sugar per 1 cc. extract
Dog 6	Salivary extract	10 cc.	Benedict's	7.4 cc.	.0004 gm.
Dog 7	Salivary extract	10 cc.	Benedict's	7.4 cc.	.0004 gm.
Cat 4	Salivary extract	20 cc.	Benedict's	6.6 cc.	.0006 gm.
Cat 5	Salivary extract	1 cc.	Benedict's	7.8 cc.	None
Cat 7	Salivary extract	10 cc.	Benedict's	7 cc.	.0008 gm.
Cat 8	Salivary extract	3 cc.	Benedict's	6 cc.	.009 gm.
Cat 9	Salivary extract	6 cc.	Benedict's	7.6 cc.	.0003 gm.
Cat 10	Salivary extract	2 cc.	Benedict's	7.6 cc.	.001 gm.
Cat 11	Salivary extract	3 cc.	Benedict's	7.8 cc.	None

TABLE VII.

Animal	Substance tested	Amt. 1 per ct. starch used	Amt. extract used	Time of digestion	Amt. 1 per ct. dextrose used	Reagent used	Amt. sugar per 1 cc. extract
Dog 5	Salivary extract	60 cc.	25 cc.	120 min.	6.4 cc.	Benedict's	0.00052 gm.
Dog 6	"	25 cc.	5 cc.	120 min.	7.2 cc.	Benedict's	0.0012 gm.
Dog 7	"	25 cc.	5 cc.	120 min.	7 cc.	Benedict's	0.0016 gm.
Cat 4	"	60 cc.	25 cc.	120 min.	6.4 cc.	Benedict's	0.00096 gm.
Cat 5	"	25 cc.	1 cc.	120 min.	7.2 cc.	Benedict's	0.008 gm.
Cat 7	"	25 cc.	2 cc.	120 min.	7.4 cc.	Benedict's	0.002 gm.
Cat 8	"	25 cc.	6 cc.	3 hrs.	7.4 cc.	Benedict's	0.0016 gm.
Cat 9	"	25 cc.	6 cc.	120 min.	6.6 cc.	Benedict's	0.002 gm.
Cat 10	"	25 cc.	2 cc.	120 min.	7.4 cc.	Benedict's	0.002 gm.
Cat 11	"	25 cc.	3 cc.	120 min.	7.4 cc.	Benedict's	0.0013 gm.

Results.—1. The salivary extract from all the animals used showed reducing substances present, except in two cats recorded in the sixth table. There is no question in my mind but that there was a reducing substance in these two cases but the failure to notice was in all probability due to the minute amount of extract used, there being only one cc. in one case and three in the other. According to the discussion in the literature[15] on the subject the reducing substance is glucose or at least it is to be inferred that it is since the saliva is shown to contain glucose.

In the first series of experiments recorded in Table I the salivary extract of four dogs and two polecats tested with a fresh Fehling's solution showed sugar to be present in every case. According to the results recorded in the second table the extract of five dogs, four of them being the same as recorded in the first, sugar was found to be present in quantities as low as 0.00064 gm. and as high as 0.0008 gm. Two cats showed 0.0024 gm. and 0.00204 gm. of sugar. Five of the seven cats and two dogs recorded in Table VI also showed sugar. The average amount is a little higher in the extract from the cat than that from the dog. Comparing the amount of sugar for each cc. of extract used as recorded in Table VI without starch and in Table VII with starch we find that there is more sugar in every case except one recorded in Table VII. The difference in every instance is marked. The two cases in which no sugar was found in the extract alone showed 0.008 and 0.0013 gm.

when digested with starch. The increase in sugar is as high as 0.0017 gm. except where no sugar was detected in the extract and there it is higher.

2. The saliva of cats after having acted on starch showed a higher percentage of sugar than the salivary extract under the same conditions and a much higher percentage than the extract not having acted on starch.

The difference in the first comparison was from 0.0003 to 0.0077 gm. of sugar. Of the four dogs recorded in Table V three produced negative results. Positive results were obtained in one case with a record of 0.002 gm. of sugar but that was after a period of seventeen and one half hours' digestion.

These results were more in accord with those of Mendel and Underhill [16] than those of Neilson and Terry.[17] One of the four dogs was kept in the kennel for at least five weeks on a diet of dog biscuit and gave a negative result.

3. With one or two exceptions the saliva, serum and salivary extracts were obtained from the same animals. The tests which have been made the determining factor are those in which the three substances last named have been taken from the same specimen. The results from serum alone and serum plus starch have been recorded in tables three and four.

In two cases where a small quantity of serum was used it took the full amount of one per cent. sugar solution to reduce 10 cc. of the copper solution. In these tests sugar was found after the action of serum upon starch. In the serum we found that sugar was present in a few instances in quantities equal to or greater than the quantity obtained from the action of saliva upon starch and in every instance the amount obtained after digesting starch with serum was greater than that obtained from saliva and starch. There is more sugar and enzyme in the serum than either salivary extract or saliva itself.

Conclusions.

I. The saliva, salivary extract and serum of the cat each contain reducing sugar.

II. The serum of both dog and cat contain a greater quantity of reducing sugar per unit volume than either the saliva or salivary extract.

III. The saliva, salivary extract and serum of the cat each showed a greater amount of reducing sugar after digesting a one per cent. starch solution.

IV. The diastatic power of blood serum is greater than that of the saliva in the cat and dog.

V. The salivary extract and serum of the dog showed diastatic power in these experiments but the saliva gave such results in only one out of four tests.

VI. The conclusions drawn are similar to those of Carlson and Luckhardt [18] that no enzymes are produced in the salivary glands of the dog and cat but are in all probability discards of the tissue in general.

Bibliography.

1. A. J. Carlson, J. R. Greer, and F. C. Becht : American Journal of Physiology, Oct. 1907. Vol. 20.

2. F. C. McLean : American Journal of Physiology, July, 1900. Vol. 22.

3. A. J. Carlson and F. C. McLean : American Journal of Physiology, January, 1908. Vol. 20.

4. A. J. Carlson and A. B. Luckhardt : American Journal of Physiology, Dec., 1908. Vol. 23.

5. Hugh C. Neilson and Oliver P. Terry : American Journal of Physiology, March, 1906. Vol. 15.

Mendel and Underhill : Journal of Biological Chemistry. Vol. III.

Neilson and Scheele. : Journal of Biological Chemistry. Vol V, 1908-09.

Neilson and Lewis : Journal of Biological Chemistry. Vol IV, 1908.

6. Neilson and Scheele. Neilson and Lewis. Neilson and Terry. Reference V.

7. Mendel and Underhill. Reference V.

8. Neilson and Lewis. Neilson and Scheele. Reference V.

9. Neilson and Terry. Mendel and Underhill. Reference V.

10. Mendel and Underhill. Reference V.

11. Neilson and Terry. Reference V.

12. A. J. Carlson and J. C. Ryan : American Journal of Physiology, April, 1908. Vol. 21.

13. A. J. Carlson and J. C. Ryan : American Journal of Physiology, July, 1908. Vol. 22.

14. Stanley R. Benedict : Journal of Biological Chemistry. Vol. III, 1907.

15. A. J. Carlson and J. C. Ryan : American Journal of Physiology, April, 1908. Vol. 21.

16. Mendel and Underhill : Journal of Biological Chemistry. Vol. III, 1907.

17. Neilson and Terry : American Journal of Physiology, March, 1906. Vol. 15.

18. A. J. Carlson and A. B. Luckhardt : American Journal of Physiology, Dec., 1908. Vol. 23.

A FLY-BLOWN AND DISTEMPERED DOG.

Pierre A. Fish.

The subject was a young collie pup four months of age. The owner suspected that the dog might be suffering from rabies from the fact that the dog had been acting in a peculiar manner for some days past. Among the symptoms noted were frothing at the mouth, howling without apparent cause, running about the fields in an excited manner apparently without purpose, and a generally wild appearance and behavior. An examination of the dog showed that in the dense hairs along the spine from the neck to the scrotum there were hundreds of maggots, many of them imbedded in the skin. The dog had evidently been fly-blown and the rabid symptoms were undoubtedly due to the pain caused by the burrowing of the maggots into the skin.

The treatment consisted in cutting the matted hair away from the infested areas and giving the dog thorough baths in a disinfectant solution of one of the coal tar products (similar to creolin). After the bath, many of the maggots came to the surface of the skin, as the disinfectant was evidently disagreeable to them. Some had burrowed so deeply or were protected from the disinfectant by the other maggots, that it was necessary to pick them out with a fine forceps to remove them.

Each day for a few days, some Sanitas soft soap was applied to the affected areas and allowed to remain for half an hour or more before being washed off. A few applications and baths were sufficient to completely remove the maggots. The cutaneous wounds were treated with a powder consisting of iodized starch and boric acid. They took on a cleaner and healthier appearance and eventually healed very nicely.

While the hair was being clipped from the body a few cutaneous eruptions were noticed along the belly. This in connection with a lack of appetite and generally depressed and emaciated condition suggested the onset of distemper. The temperature was not found above normal. A good dose of calomel, santonin, podophyllin

and sodium bicarbonate was given with the idea of thoroughly cleansing the intestinal tract and removing any worms that might be present. No worms were found.

Further treatment consisted of the administration of one dram doses of the fluidextract of Echinacea or Echafolta, twice daily. These preparations are relatively non-toxic and either of them may be administered in dram doses with impunity.

The patient received treatment for two weeks and made an excellent and complete recovery.

BLOOD EXAMINATION OF DERMATOSES IN DOGS.

Howard Welch.

This work was undertaken with a view to determining the condition of the blood of dogs suffering from the various dermatoses, both parasitic and non-parasitic in nature.

Investigations of the various skin diseases in man have established definite changes in the blood, which can be best illustrated by the following taken from Cabot:

Diseases	Leucocytes	Eosinophiles per cent	Reporter
Psoriasis	8,600	9.8	Zappert
Scleroderma	16,690	9.4	Zappert
Scleroderma	9,000	7.7	Zappert
Chronic Eczema	8,600	9.9	Zappert
Chronic Eczema	——	22	Brown
Chronic Eczema	——	45	Bettmann
Herpes tonsurans	13,000	15-24	Andry
Pemphigus	5,300	33	Zappert
Pemphigus	10,600	14.1	Zappert
Pemphigus	1,640	29	Zappert

Assuming that the normal number of leucocytes per cu. mm. is about 7,000 and that the eosinophile percentage is from 1%-4%, the above table shows conclusively a leucocytosis and an eosinophilia in the diseases quoted. In work on domestic animals suffering from dermatitis the following cases are cited (Burnett):

Diseases	Animal	Leucocytes	Eosinophilia	Reporter
Herpes tonsurans	Horse	8,500	5.4%	Meier
Mange	Dog	10,888	11	Burnett & Traum
Eczema	Dog	13,055	22	Burnett & Traum
Mange	Dog	7,899	5.3	Burnett & Traum

Here we have similar conditions existing: a leucocytosis and an eosinophilia. To determine whether or not these blood changes were constant, the following cases of dermatitis were examined.

The diagnosis of each case was based on a microscopic examination of skin scrapings in 10% caustic potash. A diagnosis of mange was made on finding the parasite of follicular mange Demodex

follicularum, or the sarcoptic parasite Sarcoptis squamiferus. In the absence of any parasite and the presence of an apparently non-contagious dermatitis, a diagnosis of eczema was made. Any condition of the animal that might influence the blood count was noted and a stool examination was made of the younger animals to determine the presence or absence of the ova of intestinal parasites. Blood was taken from the inside of the ear, with the usual precautions, and counted with Thoma's hemocytometer, using the chamber with the Zappert Ewing ruling.

The percentage of the varieties of leucocytes was determined by a count of not less than 500 cells.

Follicular Mange.

Severe Cases.

Case 1. Brindle and white bull terrier, male, 1 year. Large areas on the forehead, cheeks, throat and shoulders were bare and scurfy. The parasite was present in abundance. Patient was very lively and bright.

Blood Count	Red Cells	6,860,000
	Leucocytes	10,000
Varieties of Leucocytes	1. Lymphocytes	16%
	2. Mononuclears	3%
	3. Polynuclears	70%
	4. Eosinophiles	11%

This count shows a slight leucocytosis and a high eosinophile percentage.

Case 2. Brindle bull terrier, 18 mo., female. The areas of infection were confined mainly to the head and neck. Patient was in good condition. No pruritus.

Blood Count	Red Cells	7,480,000
	Leucocytes	8,000
	1. Lymphocytes	30%
	2. Mononuclears	5%
	3. Polynuclears	60%
	4. Eosinophiles	5%

This blood count is practically that of a normal dog.

Case 3. Brindle English bull, 2 years, male. Badly affected with the pustular form of mange. The skin on the neck, head, shoulders and flank was thick, bare and suppurating. The patient was marasmic and dull. Three blood counts were taken which show a leucocytosis and persistent eosinophilia.

	Nov. 19	Nov. 21	Dec. 1
Red Cells	6,185,000	5,800,000	6,200,000
Leucocytes	12,000	12,000	14,000
1. Lymphocytes	23%	19%	26%
2. Mononuclears	4%	6%	2%
3. Polynuclears	60%	66%	65%
4. Eosinophiles	8%	9%	7%

Case 4. White English bull, male, 2 years. The areas of infection were on the cheeks, throat, shoulders, flanks, and interior surfaces of legs. Pruritus was entirely absent.

	Jan. 10	Jan. 29
Red Cells	7,200,000	6,000,000
Leucocytes	14,000	9,000
1. Lymphocytes	26%	34%
2. Mononuclears	.3%	2%
3. Polynuclears	62%	57%
4. Eosinophiles	8%	7.5%

This shows a slight leucocytosis and eosinophilia.

Case 5. Foxhound, male, 2 months. Practically the whole body was infested with the parasite, though a case of only two weeks' standing. The parasite, though widespread, was not very abundant. No blood count taken.

Varieties of Leucocytes	1. Lymphocytes	38%
	2. Mononuclears	2%
	3. Polynuclears	56%
	4. Eosinophiles	5%

Case 6. Brindle bull terrier, male, 1 year. The forehead, jaws, cheeks and neck were devoid of hair; the skin was thick and scurfy. Both eyes were involved and suppurating.

	Feb. 12	Feb. 15
Red Cells	7,020,000	....
Leucocytes	12,800	....
1. Lymphocytes	22%	19%
2. Mononuclears	1%	3%
3. Polynuclears	64%	64%
4. Eosinophiles	13%	14%
5. Mast Cells	.4%	.2%

In this case there was a pronounced eosinophilia, with a few mast cells which are of rare occurrence in the dog.

Case 7. White bull terrier, 2 years, male. The whole fore part of body was affected badly.

Red Cells	7,520,000
Leucocytes	20,000
1. Lymphocytes	30%
2. Mononuclears	5%
3. Polynuclears	59%
4. Eosinophiles	4%

A long standing case showing a high leucocytosis. The eosinophile percentage is normal, but the number of eosin cells per cu. mm. is as high as in the preceding cases.

Case 8. Brindle Boston bull, male, 1 year. Practically the whole body was denuded of hair; the skin was thickened and pustular. The feet and legs were swollen. A bad case of mange showing a typical blood count: a high leucocyte count and an eosinophilia.

Blood Count	Red Cells	6,582,000
	Leucocytes	18,000
	1. Lymphocytes	38%
	2. Mononuclears	2%
	3. Polynuclears	51%
	4. Eosinophiles	8%

Light Cases.

Case 9. Dog, 1 year old, male. Small areas along the lips and on the cheeks were noticeable.

Blood Count	Red Cells	7,260,000
	Leucocytes	8,000
	1. Lymphocytes	35%
	2. Mononuclears	3%
	3. Polynuclears	60%
	4. Eosinophiles	2%

In this case and the following four we have a practically normal blood count.

Case 10. Scotch collie, female. A small, barely noticeable area existed on the side of the forehead. No other infection was seen.

Blood Count	Red Cells	6,428,000
	Leucocytes	14,600
	1. Lymphocytes	21%
	2. Mononuclears	4%
	3. Polynuclears	73%
	4. Eosinophiles	1%

The patient was convalescent from an ovariotomy operation which accounts for the leucocytosis.

Case 11. Gordon setter, male, 1 year. Small areas were present on the side of the head and jaw. No blood count was taken.

Differential Count of Leucocytes	1. Lymphocytes	24%
	2. Mononuclears	4%
	3. Polynuclears	70%
	4. Eosinophiles	2%

Case 12. Boston bull, male, 6 months. Small areas of infection appeared above one eye and another on the cheek. No blood count was taken.

Differential Count	1. Lymphocytes	35%
	2. Mononuclears	2%
	3. Polynuclears	60%
	4. Eosinophiles	3%

TABLE OF FOLLICULAR MANGE CASES.

SEVERE CASES.

No. & Date	Dog	Age	Red Cells	Leucocytes	Varieties of Leucocytes I Lymphocytes	II Mononuclears	III Polynuclears	IV Eosinophiles	V Mast Cells	Hb.	Area Affected
1 20-X-08	Bull Terrier	1 yr.	6,860,000	10,000	16% 1,600	3% 300	70% 7,000	11% 1,100	0 0	---- ----	Head, Shoulders and Neck
2 9-I-08	Bull Terrier	18 mo.	7,480,000	8,000	30% 2,400	5% 400	60% 4,800	5% 400	0	----	Head aud Neck
3 I-08	English Bull	2 yr.	6,185,000	12,000	23% 2,760	4% 480	60% 7,200	8% 960	.4% 5	.90	Whole Body
4 I-09	English Bull	2 yr.	7,200,000	14,000	26% 3,640	3% 420	62% 8,680	8% 1,120	0 0	.90	Head, Shoulders and Flanks
5 I-09	Foxh'nd	2 mo.	--------	-----	38% ----	2% ---	56% ------	5% -----	0	----	Whole Body
6 II-09	Bull Terrier	1 yr.	7,020,000	12,800	22% 2,810	1% 128	64% 8,200	13% 1,664	.4 5	---- ----	Head Neck : Back
7 IV-09	Bull Terrier	1 yr.	7,520,000	20,000	30% 6,000	5% 1000	59% 11,800	4% 800	--	----	Head, Neck, Shoulders, Le
8 V-09	Boston Bull	1 yr.	6,582,000	18,000	38% 6,200	2% 360	51% 9,180	8% 1,440	--	----	Whole Body

TABLE OF FOLLICULAR MANGE CASES.

LIGHT CASES.

·. & ·te	Dog	Age	Red Cells	Leucocytes	Varieties of Leucocytes I Lymphocytes	II Mononuclears	III Polynuclears	IV Eosinophiles	V Mast Cells	Hb.	Area Affect
9 15-I-08	Terrier	1 yr.	7,260,000	8,000	35% 2,800	3% 240	60% 4,800	2% 160	--	----	Side of Jaw
10 19-II-09	Collie	8 wks.	6,428,000	14,600	21% 3,060	4% 570	73% 1,060	1% 146	--	----	Side of Forehead
11 20-III-09	Setter	18 mo.	--------	------	24% ----	4% ---	70% ----	2% ----	--	----	Side of Forehead
12 8-IV-09	Boston Bull	6 mo.	--------	------	35% ----	2% ---	60% ----	3% ----	--	----	Forehead and Eyebrows

Comparing the severe with the light cases (which we may practically regard as normal animals) the blood counts show a pronounced leucocytosis. Assuming the normal leucocyte count to be 8,000 per cu. mm. (Burnett & Traum), in the eight generalized cases in the above table, only one (No. 2) is normal, and the highest is 20,000 (No. 7).

The eosinophiles likewise are high. Burnett estimates the normal number at 6%, or 480 cells per cu. mm. In the eight cases, only one (No. 2) is normal. The other seven cases show from two to three times the normal number of eosinophiles. These changes in the blood could not be attributed to any cause other than the dermatitis.

Sarcoptic Mange.

Severe Cases.

Case 13. Black Persian kitten, 2 months. The head and ears were badly affected, also slight areas on the neck. The eyes were involved. The patient was very restless and was continually scratching and rubbing the affected parts. Three counts were taken.

	Dec. 1	Dec. 2	Dec. 4
Red Cells	8,300,000	....	6,500,000
Leucocytes	26,000	....	25,000
1. Lymphocytes	21%	20%	13%
2. Mononuclears	2%	1%	1%
3. Polynuclears	46%	53%	60%
4. Eosinophiles	30%	27%	25%
5. Mast Cells	.5%	1%	1%

Case 14. Collie, male, 2 months. The head and ears were badly affected; the elbows and abdomen were also infected. The ears were devoid of hair and greatly thickened with exudate and scurf. The parasites were readily found. Considerable pruritus was evident.

Red Cells	6,500,000
Leucocytes	14,600
1. Lymphocytes	20%
2. Mononuclears	2%
3. Polynuclears	72%
4. Eosinophiles	6%

Here we have a leucocytosis and a slight rise in eosinophiles.

Case 15. Collie, male, 2 months. The whole body was more or less involved. The legs, flanks, neck and ears were scurfy and the hair quite scant. There was constant rubbing and scratching.

Red Cells	5,576,000
Leucocytes	8,000
1. Lymphocytes	14%
2. Mononuclears	4%
3. Polynuclears	74%
4. Eosinophiles	8%

This dog also had distemper, which introduces a new factor to disturb the blood count. However, an eosinophilia was present.

Case 16. Scotch collie, male, 6 weeks. The entire body was involved. Intense itching was evidenced by almost incessant scratching and rubbing. A count was taken when the case was first brought in, and another when the patient was discharged cured.

	Dec. 13	March 1
Red Cells	6,260,000	....
Leucocytes	13,000	....
1. Lymphocytes	36%	32%
2. Mononuclears	1%	4%
3. Polynuclears	44%	54%
4. Eosinophiles	17%	7%

We observe here, with the removal of the dermatitis, a drop in the eosin count from 17% to 7%.

Case 17. Maltese cat, female, 1 year. The head and ears were bare and inflamed. The patient continually rubbed and scratched the affected parts.

Red Cells	8,992,000
Leucocytes	18,200
1. Lymphocytes	8%
2. Mononuclears	1%
3. Polynuclears	82%
4. Eosinophiles	9%

Another case of mange in a cat, showing leucocytosis and eosinophilia.

Light Cases.

Case 18. English pointer, female, 2 years. There were scurfy areas on the elbows and flanks. There was a moderate amount of pruritus.

Red Cells	7,840,000	
Leucocytes	20,000	(convalescent from operation)
1. Lymphocytes	23%	
2. Mononuclears	2%	
3. Polynuclears	72%	
4. Eosinophiles	3%	

Case 19. Foxhound, female, 5 months. A very mild case; there were small areas of infection around the base of the ears.

Red Cells	6,182,000
Leucocytes	8,110
1. Lymphocytes	32%
2. Mononuclears	3%
3. Polynuclears	60%
4. Eosinophiles	4%

These light cases give the blood counts of normal dogs.

Case 20. English bull, male, 1 month. The patient was in very poor condition. The elbows and flanks were scurfy. Examination of the feces showed the presence of large quantities of the intestinal parasite Ascaris. Rachitis was also present.

Red Cells	5,696,000
Leucocytes	9,860
1. Lymphocytes	35%
2. Mononuclears	8%
3. Polynuclears	56%
4. Eosinophiles	1%

The eosinophiles were almost absent in this case, which is rather remarkable, as it is usually conceded that intestinal parasites produce an eosinophilia. A subsequent blood count showed no material change.

Cases 21, 22, 23. These three cases were mongrel collie puppies of the same litter, and all similarly affected. There were slight areas of mange at the base of the ears and on the head. Examination of the feces showed the ova of the intestinal parasites Ascaris and the hookworm (Uncinaria).

	21	22	23
Red Cells	4,320,000	5,224,000	4,472,000
Leucocytes	6,880	8,220	6,600
1. Lymphocytes	43%	37%	38%
2. Mononuclears	3%	2%	3%
3. Polynuclears	50%	61%	55%
4. Eosinophiles	3%	.4%	4%
Hemoglobin	45%	27%	54%

These counts show an anemia which is similar to that of Unicinariasis in man (Stiles), but they lack the eosinophilia conceded to such cases.

SARCOPTIC MANGE.

SEVERE CASES.

No. & Date	Dog	Age	Red Cells	Leucocytes	Varieties of Leucocytes I Lymphocytes	II Mononuclears	III Polynuclears	IV Eosinophiles	V Mast Cells	Hb.	Extent of Infection
13 1-XII-08	Persian Cat	2 mo.	8,300,000	26,000	20% 5,200	1% 260	53% 1,380	27% 7,020	1 260	100	Head and Neck
14 XII-08	Collie	2 mo.	6,500,000	14,600	20% 2,900	2% 290	72% 11,500	6% 876	--	----	Head and Ears
5 XII-08	Collie	2 mo.	5,576,000	8,000	14% 1,120	4% 320	74% 5,920	8% 640	--	90	Head, Elbows Flanks
6 I-09	Collie	6 wks.	6,260,000	13,000	36% 4,600	1% 130	44% 5,720	17% 2,200	--	90	Whole Body
ount I-09	Collie	6 wks.	--------	----	32% ----	4% ---	54% ----	7% ----	--	----	Practically Cured
7 II-09	Maltese Cat	1 yr.	8,992,000	18,200	8% 1,450	1% 182	83% 15,106	9% 1,630	--	----	Head, Ears Neck

SARCOPTIC MANGE.

LIGHT CASES.

·. & ·te	Dog	Age	Red Cells	Leucocytes	Varieties of Leucocytes I Lymphocytes	II Mononuclears	III Polynuclears	IV Eosinophiles	V Mast Cells	Hb.	Extent of Infection
·8 ·II-09	English Pointer	2 yr.	7,840,000	20,000	23% 4,600	2% 400	72% 14,400*	3% 600	--	100	Elbows & Fl·
19 14-II-09	Foxhound	5 mo.	6,182,000	8,110	32% 2,600	3% 240	60% 4,850	4% 320	--	----	Base of Ears
20 18-II-09	English Bull	1 mo.	5,696,000	9,860	35% 3,420	8% 780	56% 5,500	1% 100	--	----	Flank and Abdomen
21 3-III-09	Collie	3 wks.	4,320,000	6,880	43% 2,950	3% 210	50% 3,440	3% 210	--	45	Base of Ears and Neck; Intestinal Parasites, Ascaris and Uncinaria
22 3-III-09	Collie	3 wks.	5,224,000	8,220	37% 3,000	2% 164	61% 5,000	4% 325	--	27	
23 3-III-09	Collie	3 wks.	4,472,000	6,600	38% 2,500	3% 198	55% 3,650	4% 260	--	54	

*Recently spayed

This table shows more clearly than the previous one the leucocytosis and eosinophilia existing in severe dermatoses. The six light cases may be regarded as normal dogs, and show by contrast with the severe cases the change in the blood in sarcoptic mange. The leucocytes are about doubled in all but one case (No. 15), and in every case the eosinophiles are above the normal. In the worst case (No. 13) the eosins are the highest, and in the next in order of severity (No. 16), the eosins are next in rank. Among the lighter cases the last three, 21, 22 and 23, are interesting because they had intestinal parasites as well as mange, but showed no eosinophilia.

Eczema Cases.

Case 24. White bull terrier, male, 1 year. Scurfy areas were present on the neck, back and rump. Some irritation was evidenced by his scratching. No parasites could be found.

Red Cells	7,500,000
Leucocytes	8,600
1. Lymphocytes	18%
2. Mononuclears	2%
3. Polynuclears	76%
4. Eosinophiles	10%

The blood of this dog is about normal but for the eosinophilia.

Case 25. Scotch collie, 9 months, male. A scurfy condition of the skin over the back, flanks and shoulders was present. No parasites could be found by repeated examination.

Differential Count	1. Lymphocytes	34%
	2. Mononuclears	4%
	3. Polynuclears	52%
	4. Eosinophiles	10%

Case 26. St. Bernard, female. The whole body was affected. There were raw exudative areas forming crusts and scales all over the extremities and body. The patient was incessantly scratching herself.

	May, 1908	Feb. 20, '09
Red Cells	6,000,000	7,000,000
Leucocytes	14,000	12,000
1. Lymphocytes	20%	25%
2. Mononuclears	4%	2%
3. Polynuclears	57%	51%
4. Eosinophiles	15%	23%
5. Mast Cells	2%	.5%

These two counts were taken nearly a year apart, but the eosinophilia persisted, though at the time of the second count the patient had only very small areas of eczema.

Case 27. Boston bull, female, 4 years. She was suffering from an exudative eczema extending over both hips and rump, and down as far as the tarsus. This was a chronic case, becoming worse in hot weather.

Red Cells	6,880,000
Leucocytes	9,100
1. Lymphocytes	14%
2. Mononuclears	2%
3. Polynuclears	76%
4. Eosinophiles	10%

This blood is practically normal except for the high eosin count.

Case 28. Black cocker spaniel, female, 3 years. This was a house dog and very fat. She suffered from a chronic eczema which disappeared entirely during the winter, and reappeared in the spring. Various small areas on the abdomen, flanks and back were raw and exudative. No blood count was taken.

Differential Count of Leucocytes	1. Lymphocytes	22%
	2. Mononuclears	2%
	3. Polynuclears	65%
	4. Eosinophiles	11%

Case 29. Brown cocker spaniel, female. Large, bare exudative areas appeared on each hip. Small areas came and went on various parts of the body. There was a great amount of itching and scratching in this and the preceding eczema cases.

Blood Count	Red Cells	6,282,000
	Leucocytes	10,000
	1. Lymphocytes	32%
	2. Mononuclears	2%
	3. Polynuclears	56%
	4. Eosinophiles	10%

In this case we have a slight leucocytosis and a high eosin count.

ECZEMA.

No. & Date	Dog	Age	Red Cells	Leucocytes	Varieties of Leucocytes I Lymphocytes	II Mononuclears	III Polynuclears	IV Eosinophiles	V Mast Cells	Hb.	Areas of Infection
24 1-II-08	Bull	1 yr.	7,500,000	8,600	18% 1,550	2% 180	76% 5,540	10% 860	--	----	Back, Neck and Rump
25 18-I-09	Collie	9 mo.	---- ----	------	34% ----	4% ----	52% ----	10% ----	--	----	Areas over whole Body
26 ay-08	St. Bernard	1 yr.	6,000,000	14,000	20% 2,800	4% 560	57% 7,900	15% 2,100	2% 280	----	Whole Body esp. Hind Parts
count b.-09	St. Bernard	2 yr.	7,000,000	12,000	25% 3,500	2% 240	51% 6,120	23% 2,750	15% 60	----	Small Areas Legs
27 IV-09	Boston Bull	4 yr.	6,880,000	9,100	14% 1,270	2% 18	76% 6,900	10% 910	--	----	Hips, Rump Hind Leg
28 IV-09	Cocker Spaniel	3 yr.	---- ----	------	22% ----	2% ----	65% ----	11% ---	--	----	Back and Fla
29 -IV-09	Cocker Spaniel	1 yr.	6,282,000	10,000	32% 3,200	2% 200	56% 5,600	10% 1,000	--	----	Hips and Ru

This table shows, like the two preceding tables, a leucocytosis and eosinophilia. The leucocytosis is not so pronounced, being almost normal in three cases, 24, 27 and 29, and in no case is it as abnormally high as in the mange cases. The eosin count is, however, uniformly high. Taking the normal per cent. as 5-6%, nearly every case is double the normal number of eosins, and the more severe the skin irritation, the higher is the eosin count.

Ewing, in regard to dermatoses in man, says, "The eosinophiles are affected not so much by any special form of cutaneous lesion as by the extent, intensity and lack of healing tendency on the part of the lesion." This statement is confirmed by nearly every one of the preceding cases, but special stress should be laid upon the "intensity of the lesion," that is, the amount of pruritis and irritation it produces. Referring to the table of follicular mange cases, we find instances where the whole body is involved, the skin thickened, the hair fallen out, yet the animals were in good spirits and condition, at most being a little dull, but in no case suffering to any extent. They seldom showed restlessness or pruritus. In these cases (3, 5 and 8) the eosin per cent. was higher than normal, but not at all in proportion to the extent of the dermatosis.

On the other hand, in the sarcoptic mange cases, where the pruritus is intense, and we get incessant scratching and great restlessness, the eosin per cent. is high, considering the extent of the dermatosis. In cases 13, 14 and 17, where only limited areas of the body were involved, the eosinophilia is as high or higher than in cases of follicular mange where the whole body was affected. This striking difference can only be attributed to the difference in the amount of irritation caused by the two manges. The eczema cases only further confirm this point. In eczema we have usually even more pruritus than in either of the preceding dermatoses, though the skin lesions are relatively insignificant. A glance at the blood counts in these cases shows a more uniformly high eosin count than in the mange cases.

If we take an average of the blood counts in the tables, the following figures result:

Disease	Red Cells	Leucocytes	Eosin Per Cent
Follicular Mange	7,006,400	13,400	8.1%
Sarcoptic Mange	6,152,000	12,200	10.3%
Eczema	6,732,200	10,700	13.6%
Normal Dog	6,000,000	8,000	6 %

This table, while hardly based on enough cases to be of much weight, shows at least for the cases examined, that the eosinophilia is independent of the extent of the skin lesions, and is highest where the intensity of the irritation is greatest.

Conclusion.

From these observations the following conclusions seem warrantable:

1. That in dermatoses in dogs, the blood shows a leucocytosis and an eosinophilia.

2. That the eosinophilia depends more upon the intensity of the dermatitis than upon the extent and nature of the disease.

In concluding I wish to express my thanks to Drs. P. A. Fish and S. H. Burnett for many valuable suggestions. I am also indebted to Dr. N. P. Hinkley, of Buffalo, in whose hospital some of the cases were examined.

Bibliography.

Burnett.—Clinical Pathology of the Blood of Animals.

Burnett & Traum.—Clinical Examination of the Blood of the Dog. Proc. A. V. M. A., 1905.

Cabot.—Clinical Examination of the Blood.

Ewing.—Clinical Pathology of the Blood.

Moore, Haring & Cady.—Clinical Examination of the Blood of the Horse. Proc. A. V. M. A., 1904.

A CASE OF AUTO-ENTERECTOMY IN THE BITCH.

Pierre A. Fish.

A collie bitch two years old had her ovaries removed through the median line operation.

Toward the evening of the second day after the operation it was noticed that the stitches in the wound had been removed and two free ends of the intestine were protruding. Immediate preparations were made for suturing the ends of the intestines. The abdominal cavity was irrigated with a dilute solution of adrenalin chloride. The protruding intestines were carefully cleaned. Each end of the intestine had a gangrenous appearance for the distance of about one inch. This tissue was cut away and the ends of the intestine were drawn together by means of Lembert's sutures, catgut being used. After thorough cleansing, the parts were carefully placed in the abdominal cavity and the wound on the median line restitched.

The patient was watched for a short time after her return to the cage. She soon exhibited signs of nausea and emesis was observed to occur. On close examination the vomitus was found to consist of some blood clots and two pieces of the intestine. One of these pieces measured fifteen inches in length and the other thirteen inches, making with the excised gangrenous portions a total of thirty inches or two and a half feet. The blood clots had undoubtedly formed in the abdominal cavity, when the intestine had been bitten off, and were swallowed along with the pieces of the intestine.

In enterectomy operations, the observation has been made by Parkes that there were better chances for recovery if not more than six inches of the intestine had been removed. It is readily obvious that the greater the amount of the intestinal tube removed, the greater would be the interference with digestive processes and body metabolism and the chances for recovery greatly diminished.